SUBJECT TO COMPLETION, DATED SEPTEMBER 18, 2018

4,411,765 Shares

Common Stock

This is the initial public offering of shares of common stock of Entasis Therapeutics Holdings Inc. We are selling 4,411,765 shares of common stock. Prior to this offering, there has been no public market for our common stock. We anticipate that the initial public offering price will be between $16.00 and $18.00 per share. We have applied to list our common stock on The Nasdaq Global Market under the symbol ''ETTX.''

We have granted the underwriters a 30-day option to purchase up to 661,764 additional shares of common stock from us to cover over-allotments at the initial public offering price, less the underwriting discounts and commissions.

We are an ''emerging growth company'' as the term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements. See the section titled ''Prospectus Summary—Implications of Being an Emerging Growth Company.''

Investing in our common stock involves risks. See ''Risk Factors'' on page 15.

Certain of our stockholders (or their affiliates), including those affiliated with certain of our directors, have indicated an interest in purchasing up to an aggregate of approximately $50.0 million of shares of our common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer, or no shares in this offering to these entities, or these entities may determine to purchase more, fewer, or no shares of common stock in this offering.

	Price to Public	Underwriting Discounts and Commissions(1)	Proceeds to Us, Before Expenses
Per share	$	$	$
Total	$	$	$

(1) See ''Underwriting'' for additional information regarding underwriting compensation.

Neither the Securities and Exchange Commission, any state securities commission nor any other regulatory body has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock on or about , 2018.

Credit Suisse **BMO Capital Markets**

SunTrust Robinson Humphrey **Wedbush PacGrow**

The date of this prospectus is , 2018.

TABLE OF CONTENTS

You should rely only on the information contained in this prospectus and any free writing prospectus prepared by or on behalf of us or to which we have referred you. Neither we nor the underwriters have authorized anyone to provide you with information that is different from that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you, and neither we nor the underwriters take responsibility for any other information others may give you. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where such offers and sales are permitted. The information in this prospectus or in any free writing prospectus is accurate only as of its date, regardless of its time of delivery or the time of any sale of shares of our common stock. Our business, financial condition, results of operations and future growth prospects may have changed since that date.

Until and including , 2018 (25 days after the date of this prospectus), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to unsold allotments or subscriptions.

For investors outside of the United States: neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus.

ABOUT THIS PROSPECTUS

On April 23, 2018, we completed the corporate reorganization described under the section titled "Corporate Reorganization," pursuant to which our existing shareholders exchanged their shares in Entasis Therapeutics Limited for the same number and classes of newly issued shares in the newly incorporated Delaware company, Entasis Therapeutics Holdings Inc. and, as a result, Entasis Therapeutics Limited became a wholly owned subsidiary of Entasis Therapeutics Holdings Inc. Entasis Therapeutics Holdings Inc. had nominal assets and liabilities and did not conduct any operations prior to the reorganization other than its incorporation.

Unless otherwise indicated or the context otherwise requires, all references in this prospectus to the terms "Entasis Therapeutics Holdings Inc.," "Entasis Therapeutics Limited," "the company," "we," "us" and "our" refer to (i) Entasis Therapeutics Limited and its wholly owned U.S. subsidiary, Entasis Therapeutics Inc., prior to the completion of our corporate reorganization and (ii) Entasis Therapeutics Holdings Inc. and its subsidiaries, Entasis Therapeutics Limited and Entasis Therapeutics Inc., after the completion of our corporate reorganization.

References in this prospectus to "ordinary shares" and "preference shares" refer to the historic share capital of Entasis Therapeutics Limited prior to the completion of the corporate reorganization. All references to "common stock" and "preferred stock" refer to the capital structure of Entasis Therapeutics Holdings Inc. upon completion of the corporate reorganization.

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., the entity whose shares of common stock are being sold in this offering.

Except as otherwise indicated or the context otherwise requires, all information included in this prospectus is presented giving effect to the corporate reorganization. See the section titled "Corporate Reorganization" for more information.

We have proprietary rights to a number of trademarks and trade names used in this prospectus which are important to our business, including Entasis Therapeutics® and the Entasis logo. All other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our consolidated financial statements and the related notes thereto and the information set forth under the sections "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in each case included in this prospectus.

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 multi-drug resistant Gram-negative bacteria. Leveraging our targeted-design platform, we have engineered and developed product candidates that target clinically validated mechanisms in order 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 multi-drug resistant infections caused by *Acinetobacter baumannii*, or *Acinetobacter*. We have completed two Phase 1 clinical trials, including one evaluating the penetration of ETX2514SUL into the lung. We have also completed enrollment of an additional Phase 1 trial in renally impaired patients. In addition, we have completed a Phase 2 clinical trial in patients with complicated urinary tract infections, or UTIs, and have received positive top-line data from this trial. We expect to receive final data from our Phase 1 trial in renally impaired patients and our Phase 2 clinical trial by the end of 2018. Based on a series of discussions with the U.S. Food and Drug Administration, or FDA, we plan to initiate a single Phase 3 clinical trial in the first quarter of 2019 with data expected in 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 multi-drug resistant gonorrhea. We have completed several Phase 1 clinical trials and a Phase 2 clinical trial of zoliflodacin in patients with uncomplicated gonorrhea and intend to initiate a Phase 3 clinical trial in 2019 with data expected in 2021. The Phase 3 clinical trial will be funded by our non-profit collaborator, the Drugs for Neglected Diseases *initiative*, or DNDi.

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 multi-drug 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 the first half of 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 of 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 multi-drug 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 current 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					▪ Initiate Phase 3 trial in 1Q 2019; data expected in 2020	Worldwide excluding Asia-Pacific(1)	zai Lab
Zoliflodacin *Oral*	Uncomplicated gonorrhea					▪ Initiate Phase 3 trial in 2019; data expected in 2021	All developed countries(2)	GARDP NIH DNDi
ETX0282CPDP *Oral*	Complicated UTIs (*Enterobacteriaceae* including ESBL-producing and CRE)					▪ Data expected in 1H 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) DNDi will fully fund the Phase 3 development program for the treatment of uncomplicated gonorrhea. DNDi 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.

ETX2514SUL

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 multi-drug resistant *Acinetobacter.* Using our targeted-design platform, we engineered ETX2514 to expand the β-lactamase coverage beyond that of currently marketed BLIs. *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 against all three of these classes of β-lactamases, most importantly Class D. Sulbactam was commonly used for the treatment of *Acinetobacter* infections until β-lactamase-mediated resistance rendered it generally ineffective. We believe that ETX2514's expanded coverage against these three classes of β-lactamases gives it the potential to restore the efficacy of sulbactam against multi-drug resistant *Acinetobacter*.

Infections caused by drug-resistant *Acinetobacter*, such as severe pneumonia, as well as bloodstream, urinary tract and wound infections, can have mortality rates approaching 50% due to the lack of treatment options available to effectively treat these patients. Based on current carbapenem resistance rates, we estimate there are between 90,000 and 120,000 hospital-treated carbapenem-resistant *Acinetobacter* infections annually in the United States and the major markets in Europe, which we regard as our initial target markets for ETX2514SUL. Increasing levels of resistance have contributed to the emergence of *Acinetobacter* strains that are resistant to commonly used classes of antibiotics and have made it challenging to develop new antibiotics to treat this pathogen. As a consequence, multi-drug resistant *Acinetobacter* infections are now routinely treated with older antibiotics, such as tigecycline, a tetracycline class antibiotic, or colistin, a polymyxin class antibiotic. Although these agents show *in vitro* potency against multi-drug resistant *Acinetobacter*, colistin's toxicity in the kidney and nervous system and tetracycline's gastrointestinal tolerability issues tend to limit effective dosing, and when combined with poor tissue penetration, particularly in the lung, contribute to reduced clinical efficacy. As a result, treatment options such as colistin are often reserved as a last-resort alternative for patients. Based on the efficacy and tolerability profile of ETX2514SUL observed to date, we believe it has the potential to improve outcomes of patients with multi-drug resistant *Acinetobacter* infections, reducing their overall mortality and accelerating their recovery and hospital discharge, leading to reduced healthcare costs.

We have completed a four-part Phase 1 clinical trial in 124 healthy volunteers and a Phase 1 clinical trial evaluating the penetration of ETX2514SUL into the lung in 30 healthy volunteers, where in both, ETX2514SUL was generally well tolerated. Based on a series of discussions with the FDA, we plan to move ETX2514SUL into a single Phase 3 clinical trial in the first quarter of 2019 and expect to receive data from the trial in 2020. To optimize our Phase 3 clinical trial, we have completed enrollment of an additional Phase 1 clinical trial to assess pharmacokinetics in renally impaired patients. In parallel with this additional Phase 1 clinical trial, we have also completed a Phase 2 clinical trial in adult patients with complicated UTIs, including acute pyelonephritis (kidney infection), to provide additional safety and pharmacokinetic data, as well as efficacy data against carbapenem-resistant pathogens. We believe the efficacy data from the single Phase 3 clinical trial, if positive, will be sufficient to support the submission of a new drug application, or NDA, to the FDA.

Because patients with *Acinetobacter* infections may be co-infected with other bacterial pathogens, we plan to administer ETX2514SUL in combination with imipenem and cilastatin, or IMI, in our clinical trials to provide broad coverage for these other pathogens. Imipenem is a carbapenem antibiotic and cilastatin is a drug that prevents the degradation of imipenem. 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 beyond *Acinetobacter* infections.

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. 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

We are collaborating with DNDi to co-develop zoliflodacin as a single dose, oral antibiotic monotherapy for the treatment of uncomplicated gonorrhea. Uncomplicated gonorrhea are *N. gonorrhoeae* infections of the urethra, cervix, pharynx or rectum, and are more common than complicated gonorrhea. We anticipate commencing the Phase 3 clinical trial in 2019 with data expected in 2021, which will be fully funded by DNDi in exchange for 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.

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 has 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%.

We are developing zoliflodacin to target bacterial gyrase in a different manner than fluoroquinolones to avoid existing antibiotic resistance, resulting in a novel compound with potent *in vitro* activity against *N. gonorrhoeae* strains, including those with high-level resistance to fluoroquinolones or ESCs. In a multi-center, randomized, open-label 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. In our Phase 1 trials, zoliflodacin as a single dose was generally well tolerated at doses we would expect to be clinically active for treating uncomplicated gonorrhea. To our knowledge, zoliflodacin is the only novel treatment in active development for the treatment of drug-resistant gonorrhea with the potential to provide an oral alternative to intramuscular injections of ceftriaxone, which can be painful and require patient monitoring by a healthcare administrator. If approved, we

believe zoliflodacin has the potential to become the recommended first-line treatment of uncomplicated gonorrhea, especially as resistance to ceftriaxone increases.

ETX0282CPDP

We are developing ETX0282CPDP, an oral fixed-dose combination of ETX0282 with cefpodoxime proxetil, or cefpodoxime, 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 multi-drug resistant *Enterobacteriaceae* infections. Cefpodoxime was once used to treat UTIs, among other indications, but its clinical utility is currently limited by β-lactamase-mediated resistance. Based on our preclinical data, we believe ETX0282 has the potential to restore the efficacy of cefpodoxime against multi-drug resistant *Enterobacteriaceae.*

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. Most UTIs are treated with existing oral therapies outside of a hospital in the community setting. However, the emergence of multi-drug 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 35% of UTIs caused by *E. coli* and 18% of UTIs caused by *Klebsiella* are resistant to fluoroquinolones. 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 used in the hospital setting as an oral step-down 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 designed to have both high oral bioavailability and broad Class A and Class C β-lactamase inhibition. In *in vitro* and *in vivo* analyses, we observed that ETX0282 potently restored the efficacy of cefpodoxime to be comparable or superior to existing IV standard-of-care 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 the first half of 2019.

NBP Program

Leveraging our targeted-design platform, we are also developing a potential new class of antibiotics with our NBP program. This 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. In our preclinical studies, a number of our NBP candidates showed activity 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 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 and its affiliates 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 of our product candidates and our preclinical program have been developed using our targeted-design 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. In contrast, our platform utilizes bacterial genomics and state-of-the-art molecular and dynamic models to design active new compounds that target validated mechanisms of resistance. Throughout the design process, we aim to maximize compound penetration into bacterial cells and incorporate predictive safety tools and pharmacodynamic modeling with the goal of optimizing efficacy and safety in the clinic. Finally, we focus our clinical development on pathogens with high unmet medical need to leverage the streamlined development and regulatory pathways available for first-in-class or best-in-class antibiotics.

Our Strategy

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

- ***Rapidly advance our lead product candidate, ETX2514SUL, through clinical trials.*** We plan to initiate a single Phase 3 clinical trial of ETX2514SUL in patients with pneumonia or bloodstream infections due to *Acinetobacter* in the first quarter of 2019, and we expect to receive data in 2020. We also plan to explore additional indications with ETX2514SUL. For example, 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.*
- ***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 2019, and we expect to receive data in 2021. This Phase 3 clinical trial will be fully funded by DNDi. 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 extended-spectrum β-lactamase, or 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 the first half of 2019.
- ***Expand our product portfolio by leveraging our targeted-design platform.*** All of our product candidates have been developed using our targeted-design platform, which provides us with the potential to further 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 a number 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 DNDi, 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 for 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.

Our Team

We are led by a team of executives who have extensive experience in anti-infective drug discovery and product development at global pharmaceutical companies, including AstraZeneca, Pfizer Inc., Merck & Co., Inc. and Novartis International AG, as well as biotechnology companies, including Alexion Pharmaceuticals, Inc. and Cubist Pharmaceuticals, Inc. (acquired by Merck). Members of our team have been involved in bringing a number of anti-infective products to approval, including Invanz, Isentress, Selzentry and Trumenba. Since our spin-out and initial funding from AstraZeneca in 2015, we have raised $81.9 million in gross proceeds from equity financings with a number of U.S. and European healthcare specialist investment firms, including Clarus Lifesciences, Novo Holdings A/S, Frazier Life Sciences, Pivotal bioVenture Partners, Sofinnova Ventures, TPG Biotechnology Partners and Eventide Gilead Fund.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making a decision to invest in our common stock. These risks are discussed more fully in the "Risk Factors" section of this prospectus. These risks include the following:

- We have a limited operating history and 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 will 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 depend to a large degree on the success of our most advanced product candidates, which are in clinical development but have not completed a Phase 3 clinical trial. If we do not obtain regulatory approval for and successfully commercialize one or more of our product candidates or we experience significant delays in doing so, we may never become profitable.
- 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 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.
- 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 face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- 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.
- We are an "emerging growth company" and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our stock may be less attractive to investors.

Corporate Information

Entasis Therapeutics Holdings Inc. was incorporated under the laws of the State of Delaware in March 2018. Our principal executive offices are located at 35 Gatehouse Drive, Waltham, Massachusetts 02451 and our telephone number is (781) 810-0120. Our website address is *www.entasistx.com*. The information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus or in deciding whether to purchase shares of our common stock.

We have two wholly owned subsidiaries, Entasis Therapeutics Limited, which was incorporated under the laws of England and Wales on March 6, 2015, and Entasis Therapeutics Inc., which was incorporated under the laws of the State of Delaware on March 11, 2015.

Corporate Reorganization

As part of the corporate reorganization that was completed on April 23, 2018, we formed Entasis Therapeutics Holdings Inc., a Delaware corporation, in March 2018. Pursuant to the terms of a corporate reorganization, the entire issued share capital of the Entasis Therapeutics Limited was exchanged for the same number and classes of newly issued shares of Entasis Therapeutics Holdings Inc. and, as a result, Entasis Therapeutics Limited became a wholly owned subsidiary of Entasis Therapeutics Holdings Inc. See the section titled "Corporate Reorganization" for more information.

Implications of Being an Emerging Growth Company

As a company with less than $1.07 billion in revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For so long as we remain an emerging growth company, we are permitted and intend to rely

on exemptions from some of the reporting requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- 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 non-binding advisory vote on executive compensation or obtain stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company 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 billion in non-convertible debt during the prior three-year period. We may choose to take advantage of some or all of the available exemptions. We have taken advantage of some reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

In addition, under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as 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 will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

THE OFFERING

Common stock offered by us	4,411,765 shares
Common stock to be outstanding immediately after this offering	12,417,026 shares
Option to purchase additional shares .	We have granted the underwriters an option for a period of 30 days from the date of this prospectus to purchase up to 661,764 additional shares of our common stock.
Use of proceeds	We estimate that the net proceeds to us from this offering will be approximately $66.3 million, assuming an initial public offering price of $17.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We currently intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows: • to fund the advancement of ETX2514SUL through a Phase 3 clinical trial; • to fund the advancement of ETX0282CPDP through a multi-part Phase 1 clinical trial; • to fund the selection of an initial clinical candidate from our NBP development program and advance it through a Phase 1 clinical trial; and • the remainder to fund other research and development activities, working capital and general corporate purposes. See the section titled "Use of Proceeds" for additional information.
Risk factors	You should read the "Risk Factors" section of this prospectus for a discussion of factors to consider carefully before deciding to invest in our common stock.
Proposed Nasdaq Global Market symbol	ETTX

Certain of our stockholders (or their affiliates), including those affiliated with certain of our directors, have indicated an interest in purchasing up to an aggregate of approximately $50.0 million of shares of our common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer, or no shares in this offering to these entities, or these entities may determine to purchase more, fewer, or no shares of common stock in this offering. Of the $50.0 million of shares, Novo Holdings has indicated an interest in purchasing an aggregate of $16.3 million of shares, $10.0 million of shares of which will be allocated by Novo to its REPAIR Impact Fund. The REPAIR Impact Fund was created by Novo Holdings with a mission to invest in companies for the specific purpose of supporting early stage programs addressing antimicrobial resistance, like our NBP program.

The number of shares of our common stock that will be outstanding after this offering is based on 8,005,261 shares of common stock outstanding as of June 30, 2018, after giving effect to the automatic conversion of all outstanding shares of our preferred stock, including the accrued dividends as of August 31, 2018, into 7,992,622 shares of our common stock upon the completion of this offering, and excludes:

- 1,168,938 shares of our common stock issuable upon the exercise of stock options outstanding under our amended and restated stock incentive plan, or our 2015 Plan, as of June 30, 2018, at a weighted average exercise price of $4.70 per share;
- 2,106,894 shares of our common stock reserved for future issuance under our 2018 equity incentive plan, or our 2018 Plan, which will become effective upon the execution of the underwriting agreement related to this offering, as well as any future increases in the number of shares of common stock reserved for issuance under our 2018 Plan;
- 243,106 shares of our common stock issuable upon the exercise of stock options to be granted under our 2018 Plan upon the pricing of this offering with an exercise price per share equal to the initial public offering price per share; and
- 140,000 shares of our common stock reserved for future issuance under our 2018 employee stock purchase plan, or our ESPP, which will become effective upon the execution of the underwriting agreement related to this offering, as well as any future increases in the number of shares of common stock reserved for issuance under our ESPP.

Except as otherwise indicated herein, all information in this prospectus, including the number of shares of our common stock that will be outstanding after this offering, assumes or gives effect to:

- the completion of our reorganization described under the section titled "Corporate Reorganization";
- the filing and effectiveness of our amended and restated certificate of incorporation immediately after the completion of this offering and the adoption of our amended and restated bylaws immediately prior to the completion of this offering;
- a 1-for-20.728 reverse stock split of our common stock effected on September 17, 2018;
- the automatic conversion of all outstanding shares of our preferred stock, including the accrued dividends as of August 31, 2018, into an aggregate of 7,992,622 shares of our common stock upon the completion of this offering;
- no purchases by certain of our stockholders (or their affiliates), including those affiliated with certain of our directors, who have indicated an interest in purchasing up to an aggregate of approximately $50.0 million of shares of our common stock in this offering;
- no exercise of the outstanding options described above; and
- no exercise of the underwriters' option to purchase additional shares of our common stock.

The number of shares of our common stock to be issued upon the conversion of all outstanding shares of our convertible preferred stock depends in part on the initial public offering price of our common stock. Holders of our convertible preferred stock are entitled to receive a cumulative preferred dividend at a fixed rate of 4.0% of the issuance price of such preferred stock annually, which aggregated equaled $8.8 million as of August 31, 2018. Upon the closing of this offering, the amount of the outstanding preferred dividend will be settled in shares of our common stock based upon the initial public offering price per share. Based upon an assumed initial public offering price of $17.00 per share, and without giving effect to further accumulation of the preferred dividend after August 31, 2018, the aggregate preferred dividend will be settled with the issuance of an aggregate of 517,692 shares of our

common stock upon the closing of this offering. For illustrative purposes only, the table below shows the number of shares of our common stock that would be issuable upon conversion of the accumulated preferred dividend at various initial public offering prices per share and the resulting total number of outstanding shares of our common stock, without giving effect to further accumulation of the preferred dividend after August 31, 2018:

Assumed Initial Public Offering Price per Share	Shares of Common Stock Issuable upon Conversion of Aggregate Preferred Dividends	Total Common Stock Outstanding After this Offering
$16.00	550,048	12,449,382
$17.00	517,692	12,417,026
$18.00	488,926	12,388,260

SUMMARY CONSOLIDATED FINANCIAL DATA

In the tables below, we provide you with our summary consolidated financial data for the periods indicated. We have derived the following summary of our consolidated statement of operations data for the years ended December 31, 2016 and 2017 from our audited consolidated financial statements appearing elsewhere in this prospectus. We have derived the following summary of our consolidated statement of operations data for the six months ended June 30, 2017 and 2018 and our consolidated balance sheet data as of June 30, 2018 from our unaudited interim consolidated financial statements appearing elsewhere in this prospectus. The unaudited interim consolidated financial statements have been prepared on a basis consistent with our audited consolidated financial statements included in this prospectus and include, in our opinion, all adjustments, consisting only of normal recurring adjustments, necessary for the fair statement of the financial information in those statements. Our historical results are not necessarily indicative of the results to be expected in the future.

You should read this consolidated summary financial data together with our consolidated financial statements and related notes to those statements, as well as the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," which are included elsewhere in this prospectus.

	Year Ended December 31,		Six Months Ended June 30,	
	2016	2017	2017	2018
	(in thousands, except share and per-share data)			
Consolidated Statement of Operations Data:				
Revenue	$ —	$ —	$ —	$ 5,000
Operating expenses:				
Research and development	15,778	25,745	10,828	18,029
General and administrative	3,326	5,599	2,103	5,766
Total operating expenses	19,104	31,344	12,931	23,795
Loss from operations	(19,104)	(31,344)	(12,931)	(18,795)
Other income:				
Grant income	—	1,396	491	2,839
Interest income	9	25	12	28
Total other income	9	1,421	503	2,867
Loss before income taxes	(19,095)	(29,923)	(12,428)	(15,928)
Provision for income taxes	—	—	—	472
Net loss	$ (19,095)	$ (29,923)	$ (12,428)	$ (16,400)
Net loss per share—basic and diluted[1]	$(4,773,750.00)	$(13,795.76)	$(30,092.01)	$(1,297.57)
Weighted-average shares outstanding—basic and diluted[1]	4	2,169	413	12,639
Pro forma net loss per share		$ (8.05)		$ (2.19)
Pro forma weighted-average shares outstanding—basic and diluted		3,715,917		7,487,569

(1) See Notes 2 and 10 to our audited consolidated financial statements and Note 6 to our unaudited interim consolidated financial statements appearing elsewhere in this prospectus for further details on the calculation of basic and diluted net loss per share.

The following table presents our consolidated summary balance sheet data:

- on an actual basis as of June 30, 2018;
- on a pro forma basis to give effect to the automatic conversion of all outstanding shares of our preferred stock, including the accrued dividends as of August 31, 2018, into an aggregate of 7,992,622 shares of our common stock upon the completion of this offering; and
- on a pro forma as adjusted basis to give further effect to our sale of 4,411,765 shares of our common stock in this offering at the assumed initial public offering price of $17.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	As of June 30, 2018		
	Actual	Pro forma	Pro forma as adjusted
		(in thousands)	
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$ 33,643	$ 33,643	$102,230
Working capital	29,718	29,718	98,683
Total assets	41,503	41,503	107,375
Total liabilities	8,507	8,507	8,129
Redeemable convertible preferred stock	104,713	—	—
Total stockholders' equity (deficit)	(71,717)	32,996	99,246

The pro forma as adjusted information discussed above is illustrative only and will depend on the actual initial public offering price and other terms of this offering determined at pricing. Each $1.00 increase or decrease in the assumed initial public offering price of $17.00 per share, the midpoint of the estimated price range set forth on the cover page of this prospectus, would increase or decrease each of cash and cash equivalents, working capital, total assets and total stockholders' equity by $4.1 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting estimated underwriting discounts and commissions. We may also increase or decrease the number of shares we are offering. Each increase or decrease of 1.0 million shares in the number of shares offered by us would increase or decrease each of cash and cash equivalents, working capital, total assets and total stockholders' equity by $15.8 million, assuming that the assumed initial public offering price remains the same, and after deducting estimated underwriting discounts and commissions.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before you invest in our common stock, you should carefully consider the risks described below together with all of the other information contained in this prospectus. If any of the following risks actually occurs, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our common stock could decline, which would cause you to lose all or part of your investment. When determining whether to invest, you should also refer to the other information contained in this prospectus, including our consolidated financial statements and the related notes thereto.

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 $19.1 million and $29.9 million for the years ended December 31, 2016 and 2017, respectively, and $16.4 million for the six months ended June 30, 2018. As of June 30, 2018, we had an accumulated deficit of $73.6 million. We have funded our operations to date primarily with proceeds from the sale of our preferred stock. 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 Drugs for Neglected Diseases *initiative*, or DNDi, and an upfront payment of $5.0 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.

The report of our independent registered public accounting firm included a "going concern" explanatory paragraph.

The report of our independent registered public accounting firm on our consolidated financial statements as of and for the year ended December 31, 2017 includes an explanatory paragraph indicating that there is substantial doubt about our ability to continue as a going concern. If we are unable to raise sufficient capital in this offering or otherwise when needed, we will need to significantly modify our operational plans to continue as a going concern. If we are unable to continue as a going concern, we might have to liquidate our assets and the values we receive for our assets in liquidation or dissolution could be significantly lower than the values reflected in our consolidated financial statements. The inclusion of a going concern explanatory paragraph by our auditors, our lack of cash resources and our potential inability to continue as a going concern may materially adversely affect our share price and our ability to raise new capital or to enter into critical contractual relations with third parties.

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 this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements through 2020. 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, including purchasers of shares of our common stock in this offering, 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 and non-profit 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.

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 multi-drug 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 multi-drug 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 as a result 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 ongoing 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 as a result 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 as a result 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 disagree 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 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; for example, ETX2514SUL may initially be approvable only for *Acinetobacter* use despite our belief that it has broader clinical utility;
- 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 multi-drug 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 multi-drug 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 or not 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. 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 or not 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 multi-drug 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 treatment pending tests to identify the particular bacterial pathogen causing the infection and its 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 particular 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;
- 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 DNDi 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 and DNDi 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 DNDi 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 DNDi 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 DNDi, DNDi will fund all of 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 or not our collaborators will devote sufficient time and resources to the planned Phase 3 clinical trials. If either Zai Lab or DNDi 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 DNDi 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 for the production of 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.

In order 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 are able to 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 a number of 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 significant 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 are able to 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 multi-drug 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 with regard to 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 are able to 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 a number of 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 a number of 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 multi-drug resistant *Acinetobacter* infections. Due to rising resistance rates, standard-of-care treatment for multi-drug 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 product candidates in clinical development that have shown *in vitro* activity against *Acinetobacter*: eravacycline, currently in a Phase 3 clinical trial, 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 intra-muscular 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 multi-drug 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 multi-drug 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 or not 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 intend to enter into new employment agreements with our executive officers that will be effective upon the

date of effectiveness of the registration statement of which this prospectus forms a part, each of them may currently terminate their employment with us at any time and will continue to be able to do so after the completion of this offering. 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 June 30, 2018, we had 34 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 large 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 a number of 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 is 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 preissuance 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 grounds that our patents do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. 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 as a result 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 a number of 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 in order 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, with regard to 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. We have not yet selected trademarks for our product candidates and have not yet begun the process of applying to register trademarks for our product candidates. 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. In the event that 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 in an effort 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 of 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.

In order 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 of 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 significant 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, as a result 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 multi-drug 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 multi-drug 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, 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. In particular, 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 in the course of 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 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, 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; 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 collaborator 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 of 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 a number of 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. For a detailed discussion of the ACA's provisions of importance to the pharmaceutical industry, as well as a description of reform legislation passed subsequent to the ACA, see the section titled "Business—Government Regulation—Healthcare Reform Efforts."

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 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, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider other legislation to repeal and replace elements of the 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 manner in which 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 in light of 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 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 manner in which 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 particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to 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 in order 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.

Risks Related to this Offering, Ownership of Our Common Stock and Our Status as a Public Company

An active trading market for our common stock may not develop and you may not be able to resell your shares at or above the initial offering price, if at all.

This offering constitutes the initial public offering of our common stock, and no public market has previously existed for our common stock. We have applied to list our common stock on The Nasdaq Global Market. Any delay in the commencement of trading of our common stock on The Nasdaq Global Market would impair the liquidity of the market for the shares and make it more difficult for holders to sell their shares of our common stock. If our common stock is listed and quoted on The Nasdaq Global Market, there can be no assurance that an active trading market for the shares will develop or be sustained after this offering is completed. The initial offering price will be determined by negotiations among the lead underwriters and us. Among the factors to be considered in determining the initial public offering price are our future prospects and the prospects of our industry in general, our revenue, net income and certain other financial and operating information in recent periods, and the market prices of securities and certain financial and operating information of companies engaged in activities similar to ours. However, there can be no assurance that, following the completion of this offering, the shares of our common stock will trade at a price equal to or greater than the public offering price.

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

The trading price of our common stock following this offering is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors

may not be able to sell their shares at or above the price paid for the shares. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this prospectus, 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;
- 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 and our business.

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 in particular, 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 the course of 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.

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 will be influenced by the research and reports that equity research analysts publish about us and our business. We do not currently have and may never obtain research coverage by equity research analysts. Equity research analysts may elect not to provide research coverage of our common stock after the completion of this offering, and such lack of research coverage may adversely affect the market price of our common stock. In the event we do have equity research analyst coverage, we will 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.

If you purchase common stock in this offering, you will suffer immediate dilution of your investment.

The initial public offering price per share of our common stock is substantially higher than the pro forma as adjusted net tangible book value per share. Therefore, if you purchase common stock in this offering, you will pay a price per share that substantially exceeds our pro forma as adjusted net tangible book value per share after this offering. Based on an assumed initial public offering price of $17.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, you will experience immediate dilution of $9.01 per share, representing the difference between our pro forma as adjusted net tangible book value per share after this offering and the assumed initial public offering price per share. After this offering, we will also have outstanding options to purchase shares of our common stock with exercise prices lower than the initial public offering price. To the extent these outstanding options are exercised, there will be further dilution to investors in this offering. For further information regarding the dilution resulting from this offering, see the section titled "Dilution" in this prospectus.

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 following this offering, the market price of our common stock could decline significantly.

Upon completion of this offering, we will have outstanding 12,417,026 shares of our common stock, based on the number of shares of common stock outstanding as of June 30, 2018 and after giving effect to the automatic conversion of all outstanding shares of preferred stock, including the accrued dividends as of August 31, 2018, into an aggregate of 7,992,622 shares of common stock upon the completion of this offering. Of these shares, the 4,411,765 shares sold in this offering will be freely tradable, except shares purchased by our affiliates, and 8,005,261 additional shares of our common stock will be available for sale in the public market beginning 180 days after the date of this prospectus 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.

In addition, promptly following the completion of this offering, we intend to file one or more registration statements on Form S-8 registering the issuance of approximately 3,658,938 shares of our common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under these registration statements on Form S-8 will be available for sale in the public market subject to vesting arrangements and exercise of options, the lock-up agreements described above and, in the case of our affiliates, the restrictions of Rule 144 under the Securities Act of 1933, as amended, or the Securities Act.

Additionally, after this offering, the holders of an aggregate of 7,992,622 shares of our common stock issuable upon conversion of all of our outstanding preferred stock, including the accrued dividends as of August 31, 2018, plus any shares of common stock paid pursuant to any dividends accruing from September 1, 2018 through the day immediately prior to the closing of this offering, 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.

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.

Upon completion of this offering, our executive officers, directors and current beneficial owners of 5% or more of our common stock and their respective affiliates will, in the aggregate, beneficially own 61.5% of our outstanding common stock, based on the number of shares of our common stock outstanding as of June 30, 2018 and after giving effect to the automatic conversion of all outstanding shares of our preferred stock, including the accrued dividends as of August 31, 2018, into an aggregate of 7,992,622 shares of our common stock upon the completion of this offering. Assuming an initial public offering price of $17.00 per share, if our existing principal stockholders and their respective affiliates purchase all of the shares of common stock they have indicated an interest in purchasing in this offering, the number of shares of common stock beneficially owned by our existing executive officers, directors and principal stockholders (and their affiliates) will, in the aggregate, increase to 84.6% of our outstanding common stock. As a result, these persons, acting together, would be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors, any merger, consolidation or sale of all or substantially all of our assets, or other significant corporate transactions. 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
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

In addition, some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially below the price at which shares are being sold in this offering and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other stockholders.

Provisions in our corporate charter documents and under Delaware law could make an 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 that will become effective upon the completion of this offering 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 manner in which 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 66⅔% 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 will provide 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 will provide 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 will further provide 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 as a result 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:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- 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 cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our share price may be more volatile. We may take advantage of some or all of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company, or 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 such time as 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 will be 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.

After the completion of this offering, we will be 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 this 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 will have broad discretion in the use of proceeds from this offering and may invest or spend the proceeds 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, including the net proceeds from this offering, 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, including the net proceeds from this offering, in a manner that does not produce income or that loses value. See the section titled "Use of Proceeds" for additional information.

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 in this offering.

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

As of December 31, 2017, we had U.S. federal, state and foreign net operating loss carryforwards, or NOLs, of $10.8 million, $11.1 million and $35.2 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 as a result of this offering 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.

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.

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.

We will incur significantly increased costs as a result of operating as a company whose common stock is publicly traded in the United States, and our management will be 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 will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will 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 eventual 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. The forward-looking statements are contained principally in the sections entitled "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business," but are also contained elsewhere in this prospectus. In some cases, you can identify forward-looking statements by the words "may," "might," "will," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue" and "ongoing," or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain. Forward-looking statements include 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 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;
- the potential purchase of shares of common stock by certain of our existing stockholders, including those affiliated with certain of our directors, in this offering;
- our estimates regarding future expenses, capital requirements and needs for additional financing; and
- our expected use of proceeds from this offering.

You should refer to the "Risk Factors" section of this prospectus for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our

forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect.

This prospectus 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 this 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.

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.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of 4,411,765 shares of our common stock in this offering will be approximately $66.3 million, or approximately $76.7 million if the underwriters exercise their option to purchase additional shares in full, assuming an initial public offering price of $17.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each $1.00 increase or decrease in the assumed initial public offering price of $17.00 per share, which is the midpoint of the range set forth on the cover page of this prospectus, would increase or decrease the net proceeds to us from this offering by $4.1 million, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. We may also increase or decrease the number of shares of common stock we are offering. Each increase or decrease of 1.0 million in the number of shares of common stock we are offering at the assumed initial public offering price would increase or decrease the net proceeds to us from this offering by $15.8 million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions.

As of June 30, 2018, we had cash and cash equivalents of $33.6 million. We currently estimate that we will use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately $50.0 million to fund the advancement of ETX2514SUL through a Phase 3 clinical trial;
- approximately $3.0 million to fund the advancement of ETX0282CPDP through a multi-part Phase 1 clinical trial;
- approximately $14.0 million to fund our NBP development program, including the selection of an initial clinical candidate and advancing it through a Phase 1 clinical trial; and
- the remainder to fund other research and development activities, working capital and other general corporate purposes.

We may also use a portion of the remaining net proceeds from this offering to in-license, acquire or invest in complementary businesses, technologies, products or assets. However, we have no current commitments or obligations to do so.

This expected use of net proceeds from this offering represents our intentions based on our current plans and business conditions, which could change in the future as our plans and business conditions evolve. For example, we currently expect that our advancement of ETX0282CPDP through a multi-part Phase 1 clinical trial and the selection of an initial clinical candidate from our NBP development program and its advancement through a Phase 1 clinical trial will be funded, in part, by our two awards from CARB-X, under which we have received aggregate financial commitments of up to $16.4 million. However, the CARB-X awards are based on estimates of development costs that we have made that may prove to be wrong, and the funding we receive under these awards may not be sufficient to cover our actual costs. In addition, some of the potential funding under our CARB-X awards is subject to the achievement of pre-specified milestones, which we may not achieve. These pre-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. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the

progress of our development, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs.

Based on our planned use of the net proceeds from this offering and our existing cash and cash equivalents, we estimate that such funds will be sufficient to fund our operations and capital expenditure requirements through 2020. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

Our management will have broad discretion in the application of the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of the net proceeds of this offering.

Pending our use of the net proceeds from this offering, we plan to invest the net proceeds in a variety of capital preservation instruments, including short-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the United States government.

DIVIDEND POLICY

We have never declared or paid a dividend, and we do not anticipate declaring or paying dividends 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."

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. Investors in this offering will only acquire, and this prospectus only describes the offering of, shares of the common stock of Entasis Therapeutics Holdings Inc. We refer to the reorganization described herein as our "corporate reorganization."

Exchange of Entasis Therapeutics Limited Shares for Entasis Therapeutics Holdings Inc. Shares

Prior to the corporate reorganization, the share capital of Entasis Therapeutics Limited was divided into ordinary shares, A preference shares, B preference shares and B-1 preference shares. On April 23, 2018, the existing shareholders of Entasis Therapeutics Limited exchanged each of these classes of shares of Entasis Therapeutics 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 shares of Entasis Therapeutics Holdings Inc. have substantially identical rights to the exchanged shares of Entasis Therapeutics Limited. As a result of the exchange, Entasis Therapeutics Holdings Inc. became the sole shareholder of Entasis Therapeutics Limited and the former shareholders of Entasis Therapeutics Limited solely hold shares of Entasis Therapeutics Holdings Inc.

Exchange of Entasis Therapeutics Limited Share Options for Entasis Therapeutics Holdings Inc. Stock Options

In connection with the corporate reorganization, Entasis Therapeutics Holdings Inc. assumed the Entasis Therapeutics Limited amended and restated stock incentive plan, and each outstanding share option to purchase ordinary shares of Entasis Therapeutics 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 Therapeutics Limited were outstanding following the assumption and conversion.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of June 30, 2018:

- on an actual basis;
- on a pro forma basis giving effect to the automatic conversion of all outstanding shares of our preferred stock, including the accrued dividends as of August 31, 2018, into an aggregate of 7,992,622 shares of our common stock upon the completion of this offering;
- on a pro forma as adjusted basis to give further effect to our sale of 4,411,765 shares of our common stock in this offering at the assumed initial public offering price of $17.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with "Selected Consolidated Financial Data," "Use of Proceeds," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes appearing elsewhere in this prospectus.

	As of June 30, 2018		
	Actual	Pro forma	Pro forma as adjusted
	(in thousands, except share and per-share data)		
Cash and cash equivalents	$ 33,643	$ 33,643	$102,230
Series A redeemable convertible preferred stock, par value $0.001; 33,499,900 shares authorized, issued and outstanding, actual; no shares authorized, issued and outstanding, pro forma and pro forma as adjusted	$ 23,866	$ —	$ —
Series B redeemable convertible preferred stock, par value $0.001; 25,000,000 shares authorized, issued and outstanding, actual; no shares authorized, issued and outstanding, pro forma and pro forma as adjusted	24,550	—	—
Series B-1 Tranche A redeemable convertible preferred stock, par value $0.001; 42,372,882 shares authorized, issued and outstanding, actual; no shares authorized, issued and outstanding, pro forma and pro forma as adjusted	24,423	—	—
Series B-1 Tranche B redeemable convertible preferred stock, par value $0.001; 54,067,796 shares authorized, issued and outstanding, actual; no shares authorized, issued and outstanding, pro forma and pro forma as adjusted	31,874	—	—
Stockholders' equity (deficit):			
Preferred stock, par value $0.001: no shares authorized, issued and outstanding, actual; 10,000,000 shares authorized, no shares issued and outstanding, pro forma and pro forma as adjusted	—	—	—
Common stock, $0.001 par value: 250,000,000 shares authorized and 12,639 shares issued and outstanding, actual; 125,000,000 shares authorized and 8,005,261 shares issued and outstanding, pro forma; and 125,000,000 shares authorized and 12,417,026 shares issued and outstanding, pro forma as adjusted	0	8	12
Additional paid-in capital	1,840	106,545	172,791
Accumulated deficit	(73,557)	(73,557)	(73,557)
Total stockholders' equity (deficit)	(71,717)	32,996	99,246
Total capitalization	$ 32,996	$ 32,996	$ 99,246

Our cash and cash equivalents and capitalization following the completion of this offering will depend on the actual initial public offering price and other terms of this offering determined at pricing. Each $1.00 increase or decrease in the assumed initial public offering price of $17.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by $4.1 million, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. Each increase or decrease of 1.0 million in the number of shares offered by us in this offering would increase or decrease the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by $15.8 million, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions. The pro forma as adjusted information is illustrative only, and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

The number of shares of common stock outstanding in the table above does not include:

- 1,168,938 shares of our common stock issuable upon the exercise of stock options outstanding under our 2015 Plan as of June 30, 2018, at a weighted average exercise price of $4.70 per share;
- 2,106,894 shares of our common stock reserved for future issuance under our 2018 Plan, which will become effective upon the execution of the underwriting agreement related to this offering, as well as any future increases in the number of shares of our common stock reserved for issuance under our 2018 Plan;
- 243,106 shares of our common stock issuable upon the exercise of stock options to be granted under our 2018 Plan upon the pricing of this offering with an exercise price per share equal to the initial public offering price per share; and
- 140,000 shares of our common stock reserved for future issuance under our ESPP, which will become effective upon the execution of the underwriting agreement related to this offering, as well as any future increases in the number of shares of common stock reserved for issuance under our ESPP.

DILUTION

If you invest in our common stock in this offering, your interest will be immediately diluted to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering. Net tangible book value or deficit per share of our common stock is determined by dividing our total tangible assets less total liabilities and preferred stock by the number of outstanding shares of our common stock.

As of June 30, 2018, we had a net tangible book deficit of $(74.4) million, or $(5,889.06) per share of our common stock. On a pro forma basis, after giving effect to the automatic conversion of all outstanding shares of our preferred stock, including accrued dividends as of August 31, 2018, as of June 30, 2018 into an aggregate of 7,992,622 shares of our common stock upon the completion of this offering, our pro forma net tangible book value would have been $30.3 million, or $3.78 per share.

After giving effect to the issuance and sale of 4,411,765 shares of our common stock in this offering at the assumed initial public offering price of $17.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of June 30, 2018 would have been $99.2 million, or $7.99 per share. This represents an immediate increase in the pro forma as adjusted net tangible book value of $4.21 per share to existing stockholders, and an immediate dilution in the pro forma as adjusted net tangible book value of $9.01 per share to investors purchasing shares of our common stock in this offering. The following table illustrates this per share dilution on a per share basis:

Assumed initial public offering price per share		$17.00
Historical net tangible book deficit per share as of June 30, 2018	$(5,889.06)	
Increase per share attributable to the pro forma adjustments described above	5,892.84	
Pro forma net tangible book value per share as of June 30, 2018	3.78	
Increase in pro forma as adjusted net tangible book value per share attributable to this offering	4.21	
Pro forma as adjusted net tangible book value per share after this offering		7.99
Dilution per share to investors purchasing shares in this offering		$ 9.01

Each $1.00 increase or decrease in the assumed initial public offering price of $17.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease our pro forma as adjusted net tangible book value after this offering by $0.33 per share, and the dilution per share to investors purchasing shares in this offering by $0.67 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. Each increase of 1.0 million in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase our pro forma as adjusted net tangible book value per share after this offering by $0.59 per share and decrease the dilution to investors purchasing shares in this offering by $0.59 per share, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions. Each decrease of 1.0 million in the number of shares offered by us, as set forth on the cover page of this prospectus, would decrease our pro forma as adjusted net tangible book value per share after this offering by $0.68 per share and increase the dilution to investors purchasing shares in this offering by $0.68 per share, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions.

If the underwriters exercise their option in full to purchase additional shares in this offering, the pro forma as adjusted net tangible book value per share after the offering would be $8.39 per share, the increase in the pro forma net tangible book value per share to existing stockholders would be $4.61 per share and the dilution to new investors purchasing shares in this offering would be $8.61 per share.

The following table summarizes, on the pro forma as adjusted basis described above, the differences between the number of shares purchased from us on an as converted basis, the total consideration paid and the weighted average price per share paid by existing stockholders and by investors purchasing shares in this offering at the assumed initial public offering price of $17.00 per share, which is the midpoint of the price range set forth on the cover page on this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us:

	Shares purchased		Total consideration		Weighted average price per share
	Number	Percent	Amount	Percent	
Existing stockholders	8,005,261	64.5%	$115,456,365	60.6%	$14.42
Investors in this offering	4,411,765	35.5	75,000,000	39.4	17.00
Total	12,417,026	100.0%	$190,456,365	100.0%	

Each $1.00 increase or decrease in the assumed initial public offering price of $17.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease the total consideration paid by investors purchasing shares in this offering by $4.4 million, and in the case of an increase, would increase the percent of total consideration paid by new investors by 1.4 percentage points, and in the case of a decrease, would decrease the percent of total consideration paid by new investors by 1.4 percentage points, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. An increase or decrease of 1.0 million in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase or decrease the total consideration paid by investors purchasing shares in this offering by $17.0 million and, in the case of an increase, would increase the percentage of total consideration paid by investors purchasing shares in this offering by 5.0 percentage points and, in the case of a decrease, would decrease the percentage of total consideration paid by investors purchasing shares in this offering by 5.9 percentage points, assuming no change in the assumed initial public offering price per share.

If the underwriters exercise their option in full to purchase additional shares in this offering, the number of shares held by existing stockholders will be reduced to 61.2% of the total number of shares to be outstanding after this offering, and the number of shares held by investors participating in this offering will be increased to 38.8% of the total number of shares to be outstanding after this offering.

The total number of shares of common stock reflected in the discussion and tables above is based on 8,005,261 shares of our common stock outstanding as of June 30, 2018 after giving effect to the automatic conversion of all outstanding shares of our preferred stock, including the accrued dividends as of August 31, 2018, into 7,992,622 shares of our common stock upon the completion of this offering, and excludes:

- 1,168,938 shares of our common stock issuable upon the exercise of stock options outstanding under our 2015 Plan as of June 30, 2018, at a weighted-average exercise price of $4.70 per share;
- 2,106,894 shares of our common stock reserved for future issuance under our 2018 Plan, which will become effective upon the execution of the underwriting agreement related to this offering, as well as any future increases in the number of shares of common stock reserved for issuance under our 2018 Plan;

- 243,106 shares of our common stock issuable upon the exercise of stock options to be granted under our 2018 Plan upon the pricing of this offering with an exercise price per share equal to the initial public offering price per share; and
- 140,000 shares of our common stock reserved for future issuance under our ESPP, which will become effective upon the execution of the underwriting agreement related to this offering, as well as any future increases in the number of shares of common stock reserved for issuance under our ESPP.

To the extent that options are exercised, new options or other equity awards are issued under our equity incentive plans, or we issue additional shares in the future, there will be further dilution to investors purchasing shares in this offering. Assuming the exercise of all of our outstanding options as of June 30, 2018 (excluding options to be granted upon the pricing of this offering), the number of shares held by existing stockholders would increase to 67.5% of the total number of shares to be outstanding after this offering, and the number of shares held by investors participating in this offering would be reduced to 32.5% of the total number of shares to be outstanding after this offering. Additionally, the total consideration paid to us by existing stockholders would be $121.0 million, or 61.7%, of the total consideration paid for our outstanding shares, and the total consideration paid to us by investors participating in this offering would be 38.3% of the total consideration paid for our outstanding shares. The weighted average price per share paid to us by existing stockholders would be $13.19 and the weighted average price per share paid to us by investors participating in this offering would not change. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

SELECTED CONSOLIDATED FINANCIAL DATA

The following tables set forth our selected consolidated financial data for the periods indicated. The following selected consolidated statement of operations data for the years ended December 31, 2016 and 2017 and the selected consolidated balance sheet data as of December 31, 2016 and 2017 are derived from our audited consolidated financial statements appearing elsewhere in this prospectus. The following selected consolidated statement of operations data for the six months ended June 30, 2017 and 2018 and the selected consolidated balance sheet data as of June 30, 2018 are derived from our unaudited interim consolidated financial statements appearing elsewhere in this prospectus. The unaudited interim consolidated financial statements have been prepared on a basis consistent with our audited consolidated financial statements included in this prospectus and include, in our opinion, all adjustments, consisting only of normal recurring adjustments, necessary for the fair statement of the financial information in those statements. The data should be read together with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and in conjunction with the consolidated financial statements, related notes and other financial information

included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results to be expected in the future.

	Year Ended December 31,		Six Months Ended June 30,	
	2016	2017	2017	2018
	(in thousands, except share and per share data)			
Consolidated Statement of Operations Data:				
Revenue	$ —	$ —	$ —	$ 5,000
Operating expenses:				
Research and development	15,778	25,745	10,828	18,029
General and administrative	3,326	5,599	2,103	5,766
Total operating expenses	19,104	31,344	12,931	23,795
Loss from operations	(19,104)	(31,344)	(12,931)	(18,795)
Other income:				
Grant income	—	1,396	491	2,839
Interest income	9	25	12	28
Total other income	9	1,421	503	2,867
Loss before income taxes	(19,095)	(29,923)	(12,428)	(15,928)
Provision for income taxes	—	—	—	472
Net loss	$ (19,095)	$ (29,923)	$ (12,428)	$ (16,400)
Net loss per share—basic and diluted[(1)]	$(4,773,750.00)	$(13,795.76)	$(30,092.01)	$ (1,297.57)
Weighted-average shares outstanding—basic and diluted[(1)]	4	2,169	413	12,639
Pro forma net loss per share		$ (8.05)		$ (2.19)
Pro forma weighted-average shares outstanding—basic and diluted		3,715,917		7,487,569

(1) See Notes 2 and 10 to our audited consolidated financial statements and Note 6 to our unaudited interim consolidated financial statements appearing elsewhere in this prospectus for further details on the calculation of basic and diluted net loss per share.

	As of December 31,		As of June 30,
	2016	2017	2018
	(in thousands)		
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$ 26,256	$ 55,101	$ 33,643
Total assets	27,069	58,794	41,503
Total liabilities	4,996	9,871	8,507
Redeemable convertible preferred stock	48,416	104,713	104,713
Total stockholders' deficit	(26,343)	(55,790)	(71,717)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

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

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 multi-drug resistant Gram-negative bacteria. Leveraging our targeted-design platform, we have engineered and developed product candidates that target clinically validated mechanisms in order 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 multi drug resistant infections caused by *Acinetobacter baumannii*, or *Acinetobacter*. We have completed two Phase 1 clinical trials, including one evaluating the penetration of ETX2514SUL into the lung. We have also completed enrollment of an additional Phase 1 trial in renally impaired patients. In addition, we have completed a Phase 2 clinical trial in patients with complicated urinary tract infections, or UTIs and have received positive top-line results. We expect to receive final data from our Phase 1 trial in renally impaired patients and our Phase 2 clinical trial by the end of 2018. Based on a series of discussions with the U.S. Food and Drug Administration, or FDA, we plan to initiate a single Phase 3 clinical trial in the first quarter of 2019 with data expected in 2020.

Zoliflodacin is a novel orally administered molecule that targets bacterial gyrase 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, which will reliably treat patients with gonorrhea, including multi-drug resistant gonorrhea. We have completed several Phase 1 clinical trials and a Phase 2 clinical trial of zoliflodacin in patients with uncomplicated gonorrhea and intend to initiate a Phase 3 clinical trial in 2019 with data expected in 2021. The Phase 3 clinical trial will be funded by our non-profit collaborator, the Drugs for Neglected Diseases *initiative*, or DNDi.

We are also developing ETX0282CPDP for the treatment of complicated urinary tract infections, or 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 multi

drug 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 the first half of 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 June 30, 2018, we have funded our operations primarily from the sale of our preferred stock and have received net cash proceeds of $104.2 million. 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 Drugs for Neglected Diseases *initiative*, or DNDi, 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 losses were $19.1 million, $29.9 million and $16.4 million for the years ended December 31, 2016 and 2017 and the six months ended June 30, 2018, respectively. As of June 30, 2018, we had an accumulated deficit of $73.6 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, following the completion of this offering, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

The Corporate Reorganization

As more fully described in the section of this prospectus titled "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. Investors in this offering will only acquire, and this prospectus only describes the offering of, shares of the common stock of Entasis Therapeutics Holdings Inc.

In connection with the corporate reorganization, Entasis Therapeutics Holdings Inc. assumed the Entasis Therapeutics Limited amended and restated stock incentive plan, and each outstanding share option to purchase ordinary shares of Entasis Therapeutics 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.

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., the entity whose shares are being offered in this offering.

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 December 2018, 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 June 30, 2018, we had received $0.6 million of funding and we had recorded $0.8 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 June 30, 2018, we had received $1.4 million in funding and we had recorded $3.5 million of grant income under this grant.

In July 2017, we entered into a collaboration agreement with DNDi for the development and commercialization of a product candidate containing zoliflodacin in certain countries. Under the terms of the collaboration agreement, DNDi will fully fund the Phase 3 clinical trial, including the manufacture and supply of the product candidate containing zoliflodacin, in uncomplicated gonorrhea. See the section titled "Business—Commercial Agreements—Collaboration Agreement with DNDi."

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 June 30, 2018, we had received a payment of $4.2 million, the $5.0 million upfront payment less applicable taxes, from Zai Lab and we had recognized revenue of $5.0 million under the agreement. See the section titled "Business—Commercial Agreements—License and Collaboration Agreement with Zai Lab" for additional information.

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 share-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, 2016 and 2017 and the six months ended June 30, 2017 and 2018:

	Year Ended December 31,		Six Months Ended June 30,	
	2016	2017	2017	2018
	(in thousands)			
Direct research and development expenses by program:				
ETX2514	$ 4,661	$11,137	$ 4,890	$ 8,593
ETX0282	2,162	5,303	1,395	3,516
Zoliflodacin	744	71	22	34
Other preclinical programs	562	1,247	434	972
Unallocated research and development expenses:				
Personnel expenses (including stock-based compensation)	5,314	5,865	3,049	3,646
Facilities, supplies and other	2,335	2,122	1,038	1,268
Total research and development expenses	$15,778	$25,745	$10,828	$18,029

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 share-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 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 primarily consists of interest earned on cash equivalents in our sweep account. Our interest income has not been significant due to low interest earned on invested balances.

Income Taxes

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

Results of Operations

Six Months Ended June 30, 2017 and 2018

The following table summarizes our results of operations for the six months ended June 30, 2017 and 2018:

	Six Months Ended June 30,	
	2017	2018
	(in thousands)	
Revenue	$ —	$ 5,000
Operating expenses:		
Research and development	10,828	18,029
General and administrative	2,103	5,766
Total operating expenses	12,931	23,795
Loss from operations	(12,931)	(18,795)
Other income:		
Grant income	491	2,839
Interest income	12	28
Total other income	503	2,867
Loss before income taxes	(12,428)	(15,928)
Provision for income taxes	—	472
Net loss	$(12,428)	$(16,400)

Revenue

We did not recognize any revenue during the six months ended June 30, 2017. We recognized revenue of $5.0 million for the six months ended June 30, 2018 associated with the upfront payment under our license and collaboration agreement with Zai Lab, which was entered into in April 2018.

Research and Development Expenses

	Six Months Ended June 30,	
	2017	2018
	(in thousands)	
Personnel expenses (including stock-based compensation)	$ 3,049	$ 3,646
Preclinical and clinical development expenses	6,741	13,115
Facilities and supplies	870	858
Other expenses	168	410
	$10,828	$18,029

Research and development expenses were $10.8 million for the six months ended June 30, 2017, compared to $18.0 million for the six months ended June 30, 2018. The increase of $7.2 million was primarily due to the following increases: $6.4 million in preclinical and clinical development expenses related to the advancement of our ETX2514SUL and ETX0282CPDP product candidates and our NBP program, $0.6 million in personnel expenses associated with higher headcount and $0.2 million in other expenses associated with higher lab costs. The increase in preclinical and clinical development expenses of $6.4 million was primarily due to the following: (1) increases of $3.4 million in clinical development costs and $3.2 million in drug manufacturing costs, offset by a decrease of $0.7 million in preclinical costs resulting from the advancement of ETX2514SUL and ETX0282CPDP during the six months

ended June 30, 2018 and (2) an increase of $0.5 million in expenses associated with our preclinical programs.

General and Administrative Expenses

	Six Months Ended June 30,	
	2017	2018
	(in thousands)	
Personnel expenses (including stock-based compensation)	$ 871	$1,620
Legal and professional fees	1,014	3,293
Other expenses	218	853
	$2,103	$5,766

General and administrative expenses were $2.1 million for the six months ended June 30, 2017, compared to $5.8 million for the six months ended June 30, 2018. The increase of $3.7 million was primarily due to the following: (1) an increase of $2.3 million in legal and professional fees associated with our corporate reorganization and our preparation for becoming a public company and the preparation, audit and review of our consolidated financial statements, (2) an increase of $0.7 million in personnel expenses due to an increase of $0.5 million in salaries and benefits resulting from higher headcount and an increase of $0.2 million in stock-based compensation expense resulting from options granted during the year ended December 31, 2017 and the six months ended June 30, 2018 and (3) an increase of $0.6 million in other expenses due to an increase of $0.3 million in value-added taxes associated with the upfront payment from Zai Lab and an increase of $0.3 million in miscellaneous expenses.

Other Income

Other income was $0.5 million for the six months ended June 30, 2017, compared to $2.9 million for the six months ended June 30, 2018. The increase of $2.4 million was primarily due to an increase in grant income of $2.3 million associated with our grant agreements with USAMRAA and the CARB-X program.

Income Taxes

Provision for income taxes was $0.5 million for the six months ended June 30, 2018, which represents Chinese withholding taxes on the upfront license fee we received under the license and collaboration agreement with Zai Lab. Other than the withholding tax for China, we have not recorded any other income tax provision (benefit) for the six months ended June 30, 2018 because we had historically incurred operating losses and we maintain a full valuation allowance against our net deferred tax assets. There was no provision for income taxes for the six months ended June 30, 2017 because we had historically incurred operating losses and we maintain a full valuation allowance against our net deferred tax assets. Our losses before income taxes were generated in the United States and the United Kingdom.

Years Ended December 31, 2016 and 2017

The following table summarizes our results of operations for the years ended December 31, 2016 and 2017:

	Year Ended December 31,	
	2016	2017
	(in thousands)	
Operating expenses:		
Research and development	$ 15,778	$ 25,745
General and administrative	3,326	5,599
Total operating expenses	19,104	31,344
Loss from operations	(19,104)	(31,344)
Other income:		
Grant income	—	1,396
Interest income	9	25
Total other income	9	1,421
Net loss	$(19,095)	$(29,923)

Research and Development Expenses

	Year Ended December 31,	
	2016	2017
	(in thousands)	
Personnel expenses (including share-based compensation)	$ 5,314	$ 5,865
Preclinical and development expenses	8,129	17,758
Facilities and supplies	1,825	1,969
Other expenses	510	153
	$15,778	$25,745

Research and development expenses were $15.8 million for the year ended December 31, 2016, compared to $25.7 million for the year ended December 31, 2017. The increase of $10.0 million was primarily due to increases of $9.6 million in preclinical and development expenses and $0.6 million in personnel expenses related to the advancement of our ETX2514SUL and ETX0282CPDP product candidates, partially offset by a decrease of $0.4 million in other expenses. The increase in preclinical and development expenses was primarily due to increases of $4.9 million in clinical development, $2.0 million in drug manufacturing, $1.7 million in preclinical studies and $1.0 million in other program costs.

General and Administrative Expenses

	Year Ended December 31,	
	2016	2017
	(in thousands)	
Personnel expenses (including share-based compensation)	$1,909	$2,231
Legal and professional fees	1,189	2,956
Other expenses	228	412
	$3,326	$5,599

General and administrative expenses were $3.3 million for the year ended December 31, 2016, compared to $5.6 million for the year ended December 31, 2017. The increase of $2.3 million was primarily due to increases of $1.8 million in legal and professional fees associated with our preparation for becoming a public company and the preparation, audit and review of our consolidated financial statements and $0.3 million in salaries and benefits resulting from higher headcount.

Other Income

Other income was $9,000 for the year ended December 31, 2016, compared to $1.4 million for the year ended December 31, 2017. The increase of $1.4 million was primarily due to grant income of $1.4 million associated with our grant agreements with USAMRAA and the CARB-X program. We did not recognize any grant income during the year ended December 31, 2016.

Income Taxes

There were no provisions for income taxes for the years ended December 31, 2016 and 2017 because we have historically incurred operating losses and we maintain a full valuation allowance against our net deferred tax assets.

Liquidity and Capital Resources

Overview

As of June 30, 2018, we have raised aggregate net cash proceeds of $104.2 million from the sale of redeemable convertible preferred stock, which we have used to fund our operations. In May 2015, we entered into a Business Transfer and Subscription Agreement with AstraZeneca. Pursuant to the terms of the agreement, we sold 33,499,900 shares of Series A redeemable convertible preferred stock to AstraZeneca in consideration for property and equipment, clinical materials, intellectual property and net cash proceeds of $23.3 million. In March 2016, we received net proceeds of $24.6 million from the sale of 25,000,000 shares of Series B redeemable convertible preferred stock. In August 2017, we received net proceeds of $24.4 million from the sale of 42,372,882 shares of Series B-1 Tranche A redeemable convertible preferred stock and in December 2017, we received net cash proceeds of $31.9 million from the closing of the sale of 54,067,796 shares of Series B-1 Tranche B redeemable convertible preferred stock. 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 DNDi and an upfront payment from Zai Lab. As of June 30, 2018, we had cash and cash equivalents of $33.6 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 $19.1 million and $29.9 million for the years ended December 31, 2016 and 2017, respectively, and $16.4 million for the six months ended June 30, 2018. As of June 30, 2018, we had an accumulated deficit of $73.6 million.

We believe that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements through 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.

Without giving effect to the anticipated net proceeds from this offering, we expect that our existing cash and cash equivalents will be sufficient to fund our operating expenses and capital expenditure requirements through March 2019. To finance our operations beyond that point, we will need to raise additional capital, which cannot be assured. We have concluded that this circumstance raises substantial

doubt about our ability to continue as a going concern within one year after the August 17, 2018 issuance date of our interim consolidated financial statements for the six months ended June 30, 2018. See Note 1 to our consolidated financial statements appearing at the end of this prospectus for additional information on our assessment.

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 incur costs as a public company that we have not previously incurred or have previously incurred at lower rates, including increased fees payable to the non-employee 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 Securities and Exchange Commission, or 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:

	Year Ended December 31,		Six Months Ended June 30,	
	2016	2017	2017	2018
	(in thousands)			
Net cash used in operating activities	$(15,953)	$(27,159)	$(13,515)	$(19,166)
Net cash used in investing activities	(140)	(286)	(5)	(253)
Net cash provided by (used in) financing activities	42,192	56,290	239	(2,039)
Net increase (decrease) in cash and cash equivalents	$ 26,099	$ 28,845	$(13,281)	$(21,458)

Operating Activities

During the six months ended June 30, 2018, operating activities used $19.2 million of cash, resulting from our net loss of $16.4 million and net cash used in operating assets and liabilities of $3.3 million, partially offset by non-cash charges of $0.6 million. Net cash used in operating assets and liabilities for the six months ended June 30, 2018 consisted primarily of a $1.8 million increase in grants

receivable, a $1.4 million increase in prepaid expenses and other assets and a $0.8 million decrease in accrued expenses. These were partially offset by a $0.7 million increase in accounts payable.

During the six months ended June 30, 2017, operating activities used $13.5 million of cash, resulting from our net loss of $12.4 million and net cash used in operating assets and liabilities of $1.4 million, partially offset by non-cash charges of $0.3 million. Net cash used in operating assets and liabilities for the six months ended June 30, 2017 consisted primarily of a $0.6 million decrease in due to related party, as a result of payments made to AstraZeneca related to our transition service agreement, a $0.5 million increase in grants receivable, a $0.4 million increase in prepaid expenses and other assets and a $0.3 million decrease in accounts payable. These were partially offset by a $0.3 million increase in accrued expenses.

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.

During the year ended December 31, 2016, operating activities used $16.0 million of cash, resulting from our net loss of $19.1 million, partially offset by non-cash charges of $0.7 million and net cash provided by changes in operating assets and liabilities of $2.4 million. Net cash provided by changes in operating assets and liabilities for the year ended December 31, 2016 consisted primarily of a $1.9 million increase in accrued expenses and a $0.6 million increase in accounts payable due to the increase in costs primarily related to clinical trial and associated drug manufacturing activities for the advancement of ETX2514 and ETX0282.

Investing Activities

During the six months ended June 30, 2018, net cash used in investing activities was $0.3 million, consisting of our purchases of property and equipment.

During the six months ended June 30, 2017, there were investing activities of $5,000, consisting of our purchases of property and equipment.

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.

During the year ended December 31, 2016, net cash used in investing activities was $0.1 million, consisting of our purchases of property and equipment.

Financing Activities

During the six months ended June 30, 2018, net cash used in financing activities was $2.0 million, which related to payments of deferred initial public offering costs.

During the six months ended June 30, 2017, net cash provided by financing activities was $0.2 million, which related to proceeds from the sale of redeemable convertible preferred stock. In March 2017, we received $0.2 million from AstraZeneca, representing a portion of the net proceeds from our issuance and sale of 33,499,900 shares of Series A redeemable convertible preferred stock. These proceeds were held by AstraZeneca pursuant to our cash management services arrangement.

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.

During the year ended December 31, 2016, net cash provided by financing activities was $42.2 million, which related to sales of redeemable convertible preferred stock. In March 2016, we issued and sold 25,000,000 shares of Series B redeemable convertible preferred stock for net proceeds of $24.6 million. We also received $17.6 million from AstraZeneca, representing a portion of the net proceeds from our 2015 issuance and sale of 33,499,900 shares of Series A redeemable convertible preferred stock. These amounts were held by AstraZeneca pursuant to our cash management services arrangement.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of June 30, 2018:

	Payments Due by Period				
	Total	Less than 1 Year	1 to 3 Years	4 to 5 Years	More than 5 Years
	(in thousands)				
Operating lease commitments[1]	$2,954	$556	$1,313	$1,085	$—
Total	$2,954	$556	$1,313	$1,085	$—

(1) Amounts in the table reflect minimum payments due for our lease with AstraZeneca for office and laboratory space, which extends through December 2022.

Except as disclosed in the table above, we have no long-term debt or capital leases and no material non-cancelable purchase commitments with service providers, as we have generally contracted on a cancelable, purchase-order basis. We enter into contracts in the normal course of business with CROs, CMOs and other third parties for clinical trials, preclinical research studies and testing and manufacturing services. These contracts are cancelable by us upon prior notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to the date of cancellation. These payments are not included in the preceding table as the amount and timing of such payments are not known.

We have not included any contingent payment obligations, such as milestone payments and royalties, in the preceding table as the amount, timing and likelihood of such payments are not known. Such contingent payment obligations are described below.

The contractual obligations table does not include any potential contingent payments upon the achievement by us of clinical, regulatory and commercial events, as applicable, or royalty payments that we may be required to make under commercial agreements we have entered into with various entities, including our Business Transfer and Subscription Agreement with AstraZeneca. We excluded the contingent payments given that the timing and amount, if any, of any such payments cannot be reasonably estimated at this time. See the section titled "Business—Commercial Agreements—Business Transfer and Subscription Agreement with AstraZeneca."

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 elsewhere in this prospectus, 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, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity 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 entity satisfies a performance obligation. We only apply the five-step model to contracts when it is probable that the entity 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, we assess 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. 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 or the licensee, 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.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with applicable vendor personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. We make estimates of our accrued research and development expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to CROs and investigative sites in connection with clinical trials as well as expenses incurred in the process of product development campaigns.

We accrue our expenses related to clinical trials based on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct research activities or manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts can depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the level of effort varies from our estimate, we will adjust the accrual accordingly. If we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. Although we do not currently anticipate the future settlement of existing accruals to differ materially from our estimates, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low for any period. There have been no material changes in estimates for the period presented in our consolidated financial statements.

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 have only issued stock-based awards with service-based vesting conditions and record the expense for these awards using the straight-line method.

Effective January 1, 2018, we adopted ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*, or ASU 2018-07, which expands the scope of Topic 718 to include share-based payment awards to nonemployees. As a result, stock-based awards granted to consultants and non-employees are accounted for in the same manner as awards granted to employees and directors as described above. Prior to the adoption of ASU 2018-07, for stock-based awards granted to consultants and non-employees, we recognized compensation expense over the period during which services are rendered by such consultants and non-employees until completed. At the end of each financial reporting period prior to completion of the service, the estimated fair value of these awards was re-measured using the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option-pricing model.

We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common stock and assumptions we make for the

expected term of our stock options, the volatility of our common stock, which is based on the historical volatility of publicly traded peer companies for the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield.

Valuation of Common Stock

As there has been no public market for our common stock to date, the estimated fair value of our common stock has been 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.

After the completion of this offering, we will determine the per share fair value of our common stock based on the closing price of our common stock as reported by The Nasdaq Global Market on the date of grant.

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

Options Granted

The following table summarizes, by grant date, the number of shares of our common stock underlying each grant and the associated per-share exercise price for options granted between January 1, 2016 and August 17, 2018:

Grant Date	Number of Shares Subject to Options Granted	Exercise Price per Share	Estimated Fair Value per Share at Grant Date[(1)]	Estimated Per-Share Fair Value of Options
October 21, 2016	181,029	$3.74	$3.74	$2.08
October 21, 2016	8,443	3.74	3.74	2.51
February 7, 2017	2,412	3.74	3.74	2.61
June 1, 2017	46,200	3.74	3.74	2.29
June 1, 2017	4,615	3.74	3.74	2.61
November 22, 2017	390,293	3.11	5.60	3.94
November 22, 2017	2,921	3.11	5.60	4.47
May 1, 2018	363,243	6.85	6.85	4.15

(1) This column represents the fair value determined for the stock-based compensation expense.

The intrinsic value of all outstanding options as of June 30, 2018 was $14.3 million, based on the estimated fair value of our common stock of $17.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, of which approximately $3.1 million related to vested options and approximately $11.2 million related to unvested options.

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 prospectus 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.

Quantitative and Qualitative Disclosures about Market Risk

Our cash and cash equivalents as of June 30, 2018 consisted of cash and sweep accounts. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of interest rates. Because of the short-term nature of the instruments in our portfolio, we would not expect a sudden change in market interest rates to have a material impact on our financial position or results of operations.

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 multi-drug resistant Gram-negative bacteria. Leveraging our targeted-design platform, we have engineered and developed product candidates that target clinically validated mechanisms in order 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 multi-drug resistant infections caused by *Acinetobacter baumannii*, or *Acinetobacter*. We have completed two Phase 1 clinical trials, including one evaluating the penetration of ETX2514SUL into the lung. We have also completed enrollment of an additional Phase 1 trial in renally impaired patients. In addition, we have completed a Phase 2 clinical trial in patients with complicated urinary tract infections, or UTIs, and have received positive top-line data from this trial. We expect to receive final data from our Phase 1 study in renally impaired patients and our Phase 2 clinical trial by the end of 2018. Based on a series of discussions with the U.S. Food and Drug Administration, or FDA, we plan to initiate a single Phase 3 clinical trial in the first quarter of 2019 with data expected in 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 multi-drug resistant gonorrhea. We have completed several Phase 1 clinical trials and a Phase 2 clinical trial of zoliflodacin in patients with uncomplicated gonorrhea and intend to initiate a Phase 3 clinical trial in 2019 with data expected in 2021. The Phase 3 clinical trial will be funded by our non-profit collaborator, the Drugs for Neglected Diseases *initiative*, or DNDi.

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 multi-drug 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 the first half of 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 of 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-lactamses, 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 multi-drug 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.

We are led by a team of executives who have extensive experience in anti-infective drug discovery and product development at global pharmaceutical companies, including AstraZeneca, Pfizer Inc., Merck & Co., Inc. and Novartis International AG, as well as biotechnology companies, including Alexion Pharmaceuticals, Inc. and Cubist Pharmaceuticals, Inc. (acquired by Merck). Members of our team have been involved in bringing a number of anti-infective products to approval, including Invanz, Isentress, Selzentry and Trumenba. Since our spin-out and initial funding from AstraZeneca in 2015, we have raised $81.9 million in gross proceeds from equity financings with a number of U.S. and European healthcare specialist investment firms, including Clarus Lifesciences, Novo Holdings A/S, Frazier Life Sciences, Pivotal bioVenture Partners, Sofinnova Ventures, TPG Biotechnology Partners and Eventide Gilead Fund.

Our Pipeline

The following table summarizes the current 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					▪ Initiate Phase 3 trial in 1Q 2019; data expected in 2020	Worldwide excluding Asia-Pacific(1)	zai Lab
Zoliflodacin *Oral*	Uncomplicated gonorrhea					▪ Initiate Phase 3 trial in 2019; data expected in 2021	All developed countries(2)	GARDP NIH DNDi
ETX0282CPDP *Oral*	Complicated UTIs (*Enterobacteriaceae* including ESBL-producing and CRE)					▪ Data expected in 1H 2019	Worldwide	Powered by CARB-X
NBP Program *IV*	Gram-negative infections (initially multi-drug resistant *Pseudomonas*)					▪ Select initial clinical candidate in 2019	Worldwide	Powered by CARB-X

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

(2) DNDi will fully fund the Phase 3 development program for the treatment of uncomplicated gonorrhea. DNDi 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 multi-drug 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 multi-drug 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. Based on a series of discussions with the FDA, we plan to move ETX2514SUL into a single Phase 3 clinical trial in the first quarter of 2019 and expect to receive data from the trial in 2020. To optimize our Phase 3 clinical trial, we have completed enrollment of an additional Phase 1 clinical trial to assess pharmacokinetics in renally impaired patients. In parallel with this additional Phase 1 clinical trial, we have also completed a Phase 2 clinical trial in adult patients with complicated UTIs, including acute pyelonephritis (kidney infection), to provide additional safety and pharmacokinetic data as well as efficacy data against carbapenem-resistant pathogens. We have received positive top-line data from the Phase 2 trial and expect to receive final data from the Phase 1 clinical trial in renally impaired patients and our Phase 2 clinical trial by the end of 2018.

The Phase 2 clinical trial was designed as a double-blind, 2:1 randomized, 80-patient trial comparing ETX2514SUL plus imipenem and cilastatin, or IMI, to placebo plus IMI. Imipenem is a carbapenem antibiotic and cilastatin is a drug that prevents degradation of imipenem. Because patients with *Acinetobacter* infections may be co-infected 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. ETX2514SUL was generally well tolerated with no serious adverse events reported. Pharmacokinetic data observed in the Phase 2 trial was consistent with the pharmacokinetic data observed in the Phase 1 clinical trial in healthy volunteers. Both clinical and microbiological success rates were similar between each arm. Three patients enrolled in the ETX2514SUL plus IMI arm had infections caused by Gram-negative organisms not sensitive to imipenem and all three infections were

successfully eradicated. Placebo plus IMI eradicated isolates in three of the five patients in the placebo arm with infections caused by imipenem-non-susceptible pathogens.

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, with the exception of 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 are *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 so as 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 DNDi to co-develop zoliflodacin in a Phase 3 clinical trial. DNDi will fund all of 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 commencing the Phase 3 clinical trial in 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 extended-spectrum β-lactamase, or ESBL, -producing bacterial strains or 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 step-down 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 the first half of 2019.

NBPs for the treatment of multi-drug 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 activity of a number of our NBPs 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 of 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 have an understanding of the way in which pathogens develop resistance. Clinically validated mechanisms means that prior drugs have been developed to target such mechanisms of antibiotic resistance, and that such drugs 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 that 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, in order 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 multi-drug resistant Gram-negative infections. Our pathogen-directed strategy includes the following key components:

- ***Rapidly advance our lead product candidate, ETX2514SUL, through clinical trials.*** We plan to initiate a single Phase 3 clinical trial of ETX2514SUL in patients with pneumonia or bloodstream infections due to *Acinetobacter* in the first quarter of 2019, and we expect to receive data in 2020. We also plan to explore additional indications with ETX2514SUL. For example, 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.*

- ***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 2019, and we expect to receive data in 2021. This Phase 3 clinical trial will be fully funded by DNDi. 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 the first half of 2019.
- ***Expand our product portfolio by leveraging our targeted-design platform.*** All of 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 a number 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 DNDi, 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, similar to 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:*** Taking into account 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

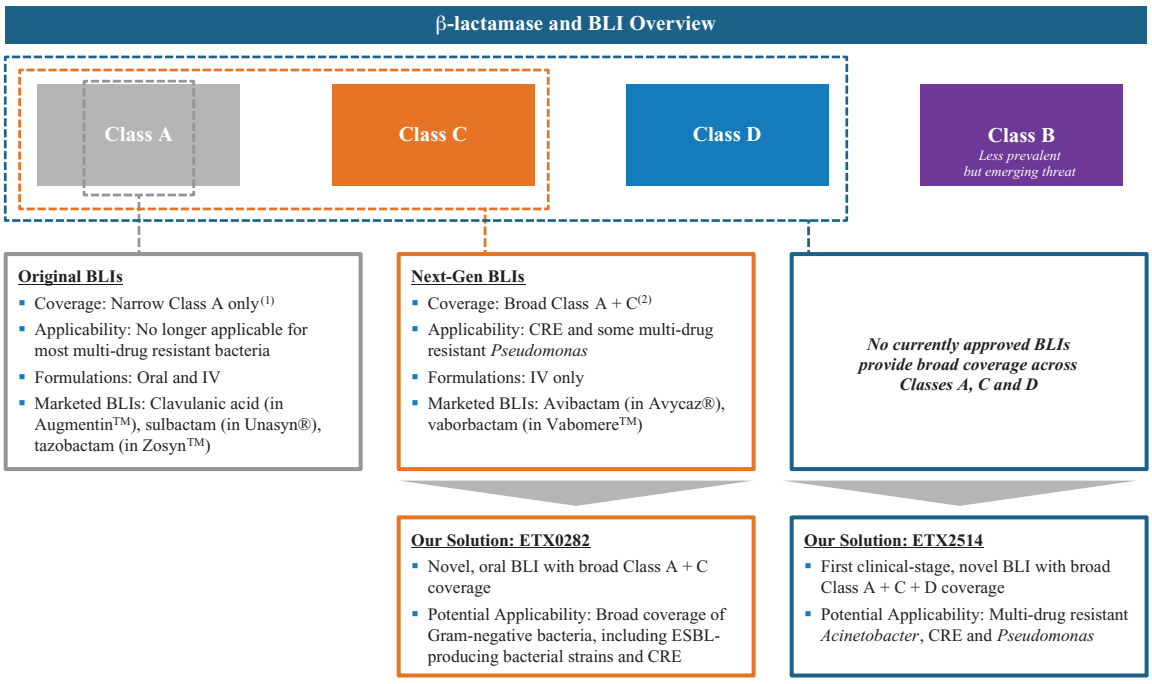
β-lactams are one of the most widely used antibiotic classes due to their attractive safety and efficacy profile. β-lactams work by inhibiting PBPs, proteins that play an important role in bacterial cell wall synthesis and are essential for the growth and reproduction of bacteria. β-lactam antibiotics 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 particular concern in infections caused by multi-drug 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 2014, surpassing 35%. *E. coli* resistance to cephalosporins quadrupled over the same period, reaching 16% in 2014. *Klebsiella* reached carbapenem- and cephalosporin-resistance of 8% and 20%, respectively, in 2014, up from 0% and 13%, respectively, in 2004. Approximately 20% of *Pseudomonas* infections are resistant to carbapenems, third-generation cephalosporins and 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 6% and 8% annually, 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, DNDi 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 multi-drug 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 stand-alone 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 multi-drug resistant *Acinetobacter*.

Because patients with *Acinetobacter* infections may be co-infected 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 multi-drug resistant and, in 2014, nearly half of *Acinetobacter* strains tested were resistant to carbapenem antibiotics, an increase from 18% in 2004. 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* among the six most threatening antimicrobial-resistant pathogens responsible for high morbidity and mortality in patients, the CDC has classified *Acinetobacter* 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 multi-drug 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. As a consequence, multi-drug 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 multi-drug 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 multi-drug 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 multi-drug 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 stand-alone 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 two Phase 1 and our Phase 2 clinical trials, including at doses that are well in excess of our expected 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 multi-drug 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, we plan to move ETX2514SUL into a single Phase 3 clinical trial in the first quarter of 2019. 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% non-inferiority margin, in the approximately 130 patients with confirmed carbapenem-resistant *Acinetobacter* infections. Non-inferiority 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, an exploratory objective will be to evaluate the clinical and microbiologic efficacy of ETX2514SUL in combination with IMI in patients co-infected 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 of 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 are undertaking 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, with the exception of 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 plan to initiate the Phase 3 clinical trial during the first quarter of 2019 and expect to receive data in 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 prelinical studies and, where available, 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. Data from our additional ongoing Phase 1 and our Phase 2 clinical trials will also be incorporated into this analysis to further refine dose setting ahead of the Phase 3 clinical trial.

Recently Completed and Additional Ongoing Clinical Trials

To optimize our Phase 3 clinical trial, we have initiated two additional Phase 1 clinical trials in the United States, one to evaluate drug penetration into the lung and one to assess pharmacokinetics in renally impaired patients. We recently completed the lung trial that 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*. The renal trial will analyze serum levels in renally impaired patients and will provide data to enable construction of a dose-adjustment protocol for these types of patients, who are also likely to be enrolled in the Phase 3 clinical trial. The Phase 1 clinical trial in renally impaired patients has completed enrollment and we expect to receive final data by the end of 2018.

In parallel with these additional Phase 1 clinical trials, we have 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. We have received top-line data from this study and expect to receive the final clinical study report by the end of 2018. The Phase 2 clinical trial is designed as a 2:1 randomized, 80-patient trial comparing ETX2514SUL plus IMI to placebo plus IMI. 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. With respect to efficacy, clinical success was 100% in both the ETX2514SUL plus IMI and placebo plus IMI arms, and overall microbiological success was 80% (36 of 45 patients) and 81% (17 of 21 patients) in the ETX2514SUL plus IMI and placebo plus IMI arms, respectively. Three patients enrolled in the ETX2514SUL plus IMI arm had infections caused by Gram-negative organisms not sensitive to imipenem and all three infections were successfully eradicated. Placebo plus IMI eradicated isolates in three of the five patients in the placebo arm with infections caused by imipenem-non-susceptible pathogens.

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. 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.

Based on a series of discussions with the FDA, 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.

Phase 1 Clinical Data

We have completed a four-part Phase 1 clinical trial in Australia in 124 healthy volunteers in which 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 3 hours every 6 hours for 8 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 6 hours over a period of 11 days, was generally well tolerated with no serious adverse events or discontinuations.

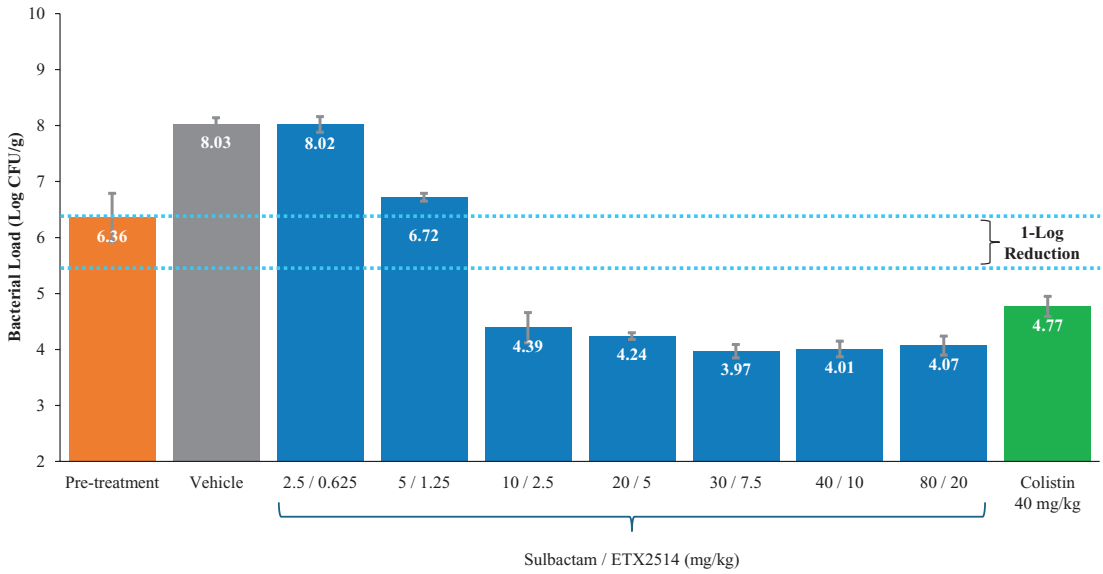
There were two drug-related discontinuations in the Phase 1 clinical trial, one mild-moderate adverse event (transient drowsiness and nausea) in the 0.5 g ETX2514 multiple ascending dose escalation cohort and one moderate adverse event (transient allergic reaction symptoms) in the 1.0 g ETX2514 multiple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

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. Our Phase 1 clinical trials are covered by this IND. The FDA granted Fast Track designation and QIDP designation for ETX2514SUL in September 2017 for the treatment of hospital-acquired and ventilator-acquired bacterial pneumonia and bloodstream infections due to *Acinetobacter*.

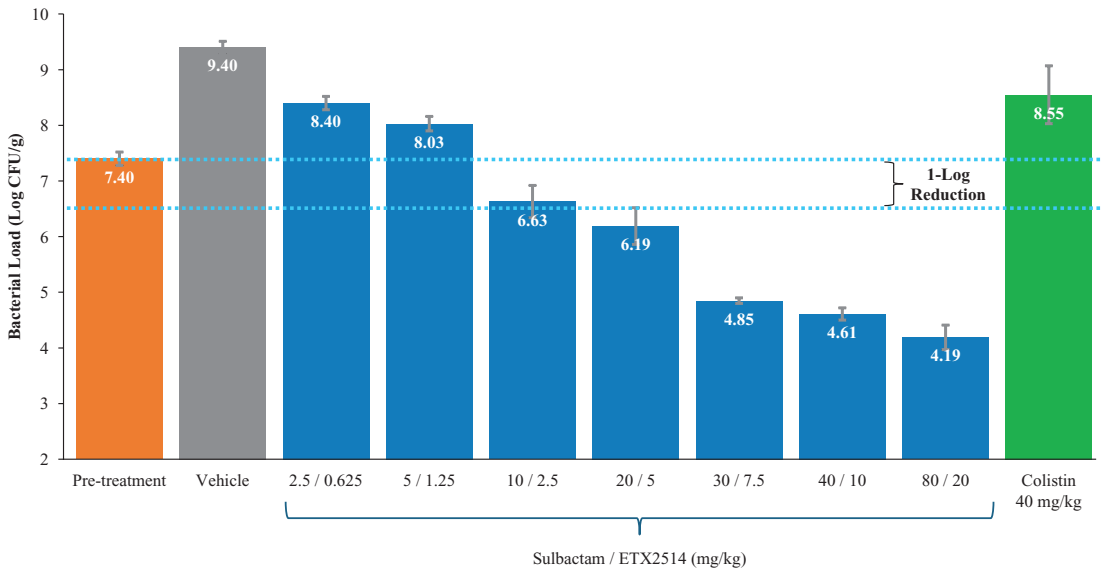
Preclinical Data

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 multi-drug 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 particular 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 3 hours every 6 hours.

***In Vivo* Activity of ETX2514 + Sulbactam in Mouse Thigh Infection Model[(1)]**



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

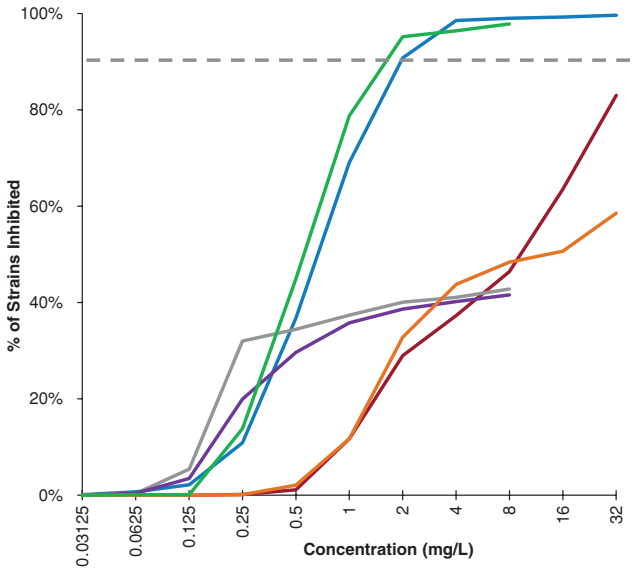


(1) ETX2514, sulbactam and colistin were dosed subcutaneously. Colistin was injected to the maximum tolerated dose.

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 3,611 recent strains of *Acinetobacter*. We tested sulbactam, ETX2514SUL, imipenem and meropenem against these strains, and amikacin and colistin against 3,003 of the 3,611 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 of 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 3,611 *Acinetobacter* Strains**



	MIC_{90} (mg/L)	CLSI Breakpoint (mg/L)
Sulbactam	64	4(1)
ETX2514SUL	**2**	**NA**
Imipenem	>8	2
Meropenem	>8	2
Amikacin (2)	>64	16
Colistin (2)	2	2

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

(2) Sulbactam, ETX2514SUL, imipenem and meropenem were tested against all 3,611 strains. Amikacin and colistin were tested against 3,003 of the 3,611 strains.

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 3,003 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*. In order 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 DNDi to co-develop zoliflodacin in a Phase 3 clinical trial for the treatment of uncomplicated gonorrhea. Uncomplicated gonorrhea are *N. gonorrhoeae* infections of the urethra, cervix, pharynx or rectum, and are more common than complicated gonorrhea. DNDi will fund all of 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 multi-drug 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 also 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 DNDi to co-develop zoliflodacin in a multinational Phase 3 clinical trial, which we anticipate initiating in 2019 with data expected in 2021. DNDi will fund all of 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.

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, non-inferiority 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 non-inferiority 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.

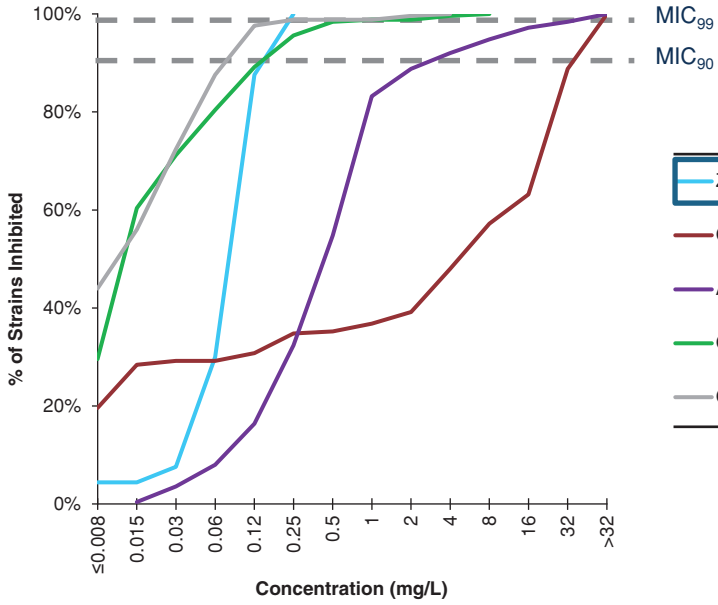
Prior to initiating the planned Phase 3 clinical trial, our new zoliflodacin granule formulation is being studied in eight subjects to assess its relative bioavailability to the prior formulation. This study will be followed by a formal Thorough QT study, which is a typical requirement for approval of a new chemical entity by the FDA. The purpose of a Thorough QT study is to determine whether a drug has an effect on cardiac rhythms.

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 planned Phase 3 clinical trial is expected to be conducted pursuant to an IND submitted by DNDi.

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**



	MIC$_{90}$ (mg/L)	MIC$_{99}$ (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 multi-drug 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 multi-drug 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 multi-drug 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 step-down 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 multi-drug 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 35% of UTIs caused by *E. coli* and 18% 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 multi-drug 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 a number of 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 multi-drug 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 full data from the Phase 1 trial in the first half of 2019. We held a pre-IND meeting with the FDA in March 2018 and are incorporating the FDA's feedback into our clinical development plans for ETX0282CPDP.

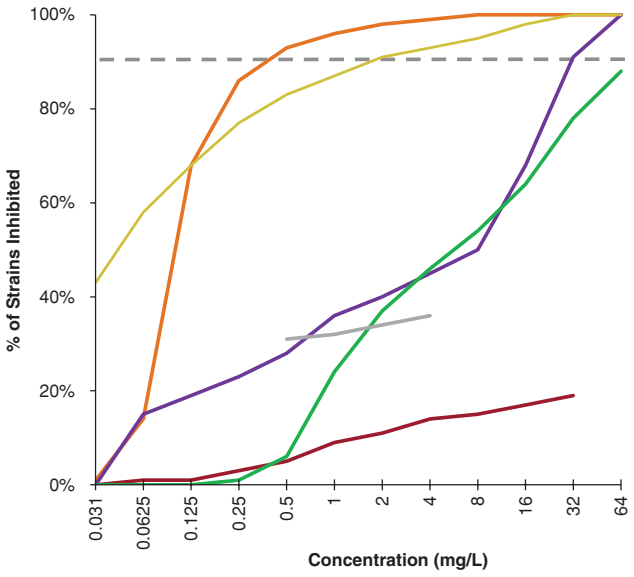
Preclinical Data

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 multi-drug 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**



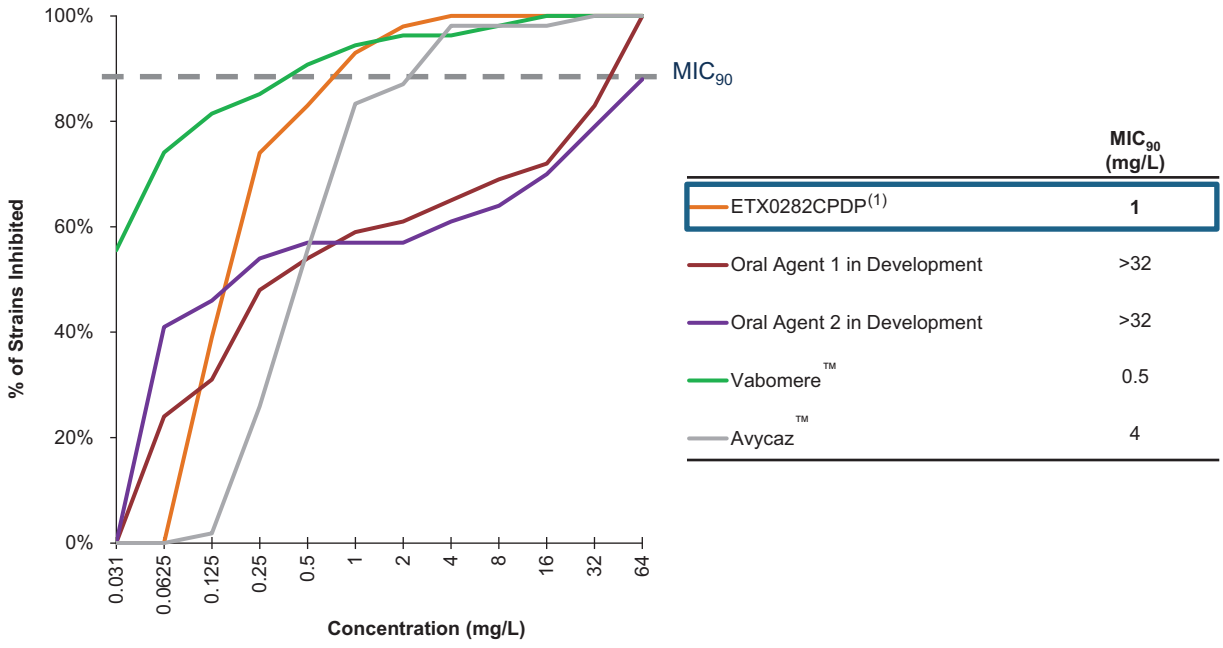
	MIC$_{90}$ (mg/L)	CLSI Breakpoint (mg/L)
Cefpodoxime	>32	2
ETX0282CPDP[(1)]	**0.5**	**NA**
Levofloxacin	32	2
Fosfomycin	>64	64
Trimethoprim / sulfamethoxazole[(2)]	ND	2
Ertapenem (Intravenous)	2	0.5

(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 multi-drug 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 strains inhibited by increasing concentrations of each of the tested compounds. Both of the 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.

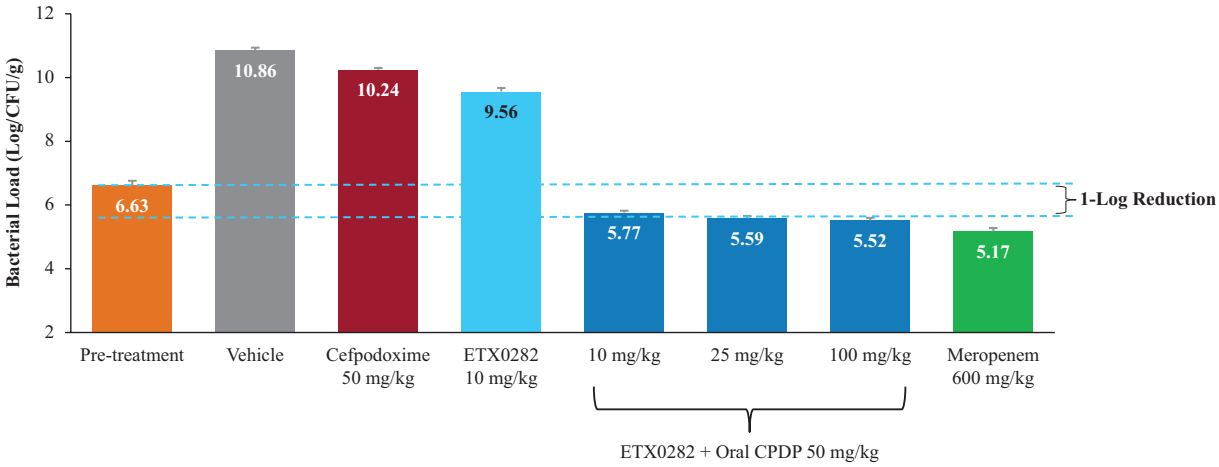
***In Vitro* Activity of ETX0282CPDP[(1)] Against 54 *Enterobacteriaceae* Strains, Including CRE**



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

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 from a number of our NBPs 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 multi-drug 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 of these 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 multi-drug 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 multi-drug resistant *Pseudomonas* and other Gram-negative pathogens. While we believe our novel NBP class may have broad antibacterial activity against a number of Gram-negative pathogens, we expect the initial clinical candidate that we select from this program will aim to address the serious medical need of multi drug-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 multi-drug 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 a number of 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 classes and have shown activity against multiple drug-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 multi-drug 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 multi-drug 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 June 30, 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 $5.9 million, with the possibility of up to a total of $16.4 million in funding based on the successful completion of pre-specified 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, two-year $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.

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 will automatically be converted into 1,616,166 shares of our common stock upon completion of this offering. 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 DNDi 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 DNDi

In July 2017, we entered into a collaboration agreement with DNDi for the development and commercialization of a product candidate containing zoliflodacin in certain countries. Under the terms of the collaboration agreement, DNDi 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 Thorough QT study on the granule formulation of zoliflodacin in collaboration with NIAID. 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 $75,000 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 DNDi a worldwide, fully paid, exclusive and royalty-free license, with the right to sublicense, to use our zoliflodacin technology in connection with DNDi's development, manufacture and commercialization of zoliflodacin in low-income and specified middle-income countries, which we refer to collectively as the DNDi 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 in order to perform our obligations under the collaboration agreement and for any purpose other than gonorrhea or community-acquired indications. DNDi will own all intellectual property developed in its performance under the collaboration agreement with regard to formulation development of zoliflodacin. To the extent DNDi 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, DNDi 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 DNDi territory where we filed patent rights at the date of the agreement and, under specified conditions, in our

territory, and DNDi must reimburse us for costs and expenses for the maintenance of such intellectual property rights in the countries of the DNDi 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 DNDi has not achieved certain clinical milestones within a specified time period, unless the non-achievement 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, less applicable taxes, from Zai Lab, and we are eligible to receive up to an aggregate of $7.6 million in near-term development milestones and research and development support payments and up to an aggregate of $91.0 million in additional 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 non-competitive before we can recover the expenses of their development commercialization.

We are initially developing ETX2514SUL for the treatment of multi-drug resistant *Acinetobacter* infections. Due to rising resistance rates, standard-of-care treatment for multi-drug 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 product candidates in clinical development that have shown *in vitro* activity

against *Acinetobacter*: eravacycline, currently in a Phase 3 clinical trial, 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 combination therapy intra-muscular 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 multi-drug 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 multi-drug 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 August 31, 2018, we owned three issued U.S. patents, 52 issued foreign patents as well as 29 pending foreign patent applications and one published Patent Cooperation Treaty, or PCT. The issued foreign patents are in a number of

jurisdictions including Australia, the European Union, China, Isreal, 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, November 2035 and May 2037.

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 August 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 a number of 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 August 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 published PCT and one provisional patent application 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 DNDi

In July 2017, we entered into a collaboration agreement with DNDi for the development and commercialization of a product candidate containing zoliflodacin in certain countries. DNDi will own all intellectual property developed in its performance under the collaboration agreement with regard to formulation development of zoliflodacin. To the extent DNDi 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, DNDi 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 DNDi territory where we had patents or had filed patent applications prior to the agreement and, under specified conditions, in our territory, and DNDi must reimburse us for costs and expenses for the maintenance of such intellectual property rights in the countries of the DNDi territory.

Trademarks, Trade Secrets and Know-How

Our trademark portfolio currently consists of registered trademark and service mark rights for ENTASIS THERAPEUTICS in a number of 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 in order 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 or not 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 makes a contribution 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 non-priority 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 in order 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. In order 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 non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent 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 of 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 non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA 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 a number of 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 of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order 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 on the other. Although there are a number of 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 of 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 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 in order 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, imposes 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 to requiring drug manufacturers to report information related to payments to clinicians and other healthcare providers or marketing expenditures. 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 agree to offer 50% (70% commencing January 1, 2019) 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 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 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, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider other legislation to repeal and replace elements of the ACA. Congress will likely consider other legislation to replace elements of the ACA.

In addition, other federal health reform measures have been proposed and adopted in the United States since the ACA was enacted. For example, as a result 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 manner in which 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. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

At the state level, legislatures 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 has to 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 in particular 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 on the basis of a re-evaluation 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 de-centralized 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 considered to be 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 10-year 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.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union (commonly referred to as "Brexit"). Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provided the notice of withdrawal pursuant to the Treaty on European Union, or on March 29, 2019. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, immediately following Brexit, it is expected that the regulatory regime will remain the same as prior to Brexit. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom. In the longer term, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom.

Employees

As of June 30, 2018, we had 34 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.

Facilities

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.

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.

MANAGEMENT

Directors and Executive Officers

The following table sets forth information concerning our directors and executive officers, including their ages as of January 1, 2018:

Name	Age	Position
Executive Officers:		
Manoussos Perros, Ph.D.	50	President, Chief Executive Officer and Director
Michael Gutch, Ph.D.	51	Chief Financial Officer and Chief Business Officer
Robin Isaacs, M.D.	59	Chief Medical Officer
John Mueller, Ph.D.	57	Chief Development Officer
Ruben Tommasi, Ph.D.	52	Chief Scientific Officer
Non-Management Directors:		
Nicholas Galakatos, Ph.D.[3]	60	Chairman of the Board of Directors
Heather Behanna, Ph.D.[1][3]	42	Director
Thomas Dyrberg, M.D., D.M.Sc.*	63	Director
David C. Hastings[1]	56	Director
Robert Hopfner, Ph.D.*	45	Director
Gregory Norden[2][3]	60	Director
Heather Preston, M.D.[2]	51	Director
Andrew J. Staples[1]	48	Director
James N. Topper, M.D., Ph.D.[2]	55	Director

* Drs. Dyrberg and Hopfner will resign from our board of directors contingent upon and effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part.

(1) Member of the audit committee

(2) Member of the compensation committee

(3) Member of the nominating and corporate governance committee

Executive Officers

Manoussos Perros, Ph.D., has served as our chief executive officer, co-founder and director since May 2015. Prior to this, Dr. Perros worked for AstraZeneca AB as vice president and head of its infection research and early development organization from 2010 to 2015 and as site head for its research center in Waltham, Massachusetts from 2012 to 2015. Prior to joining AstraZeneca, Dr. Perros served as director of the Novartis Institute for Tropical Diseases in Singapore, and prior to that, as vice-president and chief scientific officer, antivirals, at Pfizer, Inc. A chemist by training, Dr. Perros conducted his Ph.D. work in Belgium, France and Germany, and was an associate in the Biophysics department at Yale from 1993 to 1995. Dr. Perros received the PhRMA Discoverer's Award in 2010. We believe that Dr. Perros is qualified to serve on our board of directors because of his extensive knowledge of our company as co-founder and chief executive officer, his experience at major pharmaceutical companies and his scientific experience and achievements.

Michael Gutch, Ph.D., has served as our chief business officer and chief financial officer since April 2017. From January 2014 to March 2017, he served as executive director of corporate development and head of equities at AstraZeneca. Dr. Gutch served as managing director, MedImmune Ventures, the corporate venture capital arm of AstraZeneca, from September 2011 to December 2013. Prior to that, Dr. Gutch served as investment director of HIG BioVentures at the investment firm HIG Capital and as a principal of Lilly Ventures, the corporate venture arm of Eli Lilly & Company. He currently serves on the boards of directors of Albireo Pharma, Inc. Dr. Gutch

received his MBA in Finance from Indiana University and a Ph.D. in Molecular Pathology from SUNY Stony Brook. He earned his B.S. degrees in Biology and Chemistry from Alfred University.

Robin Isaacs, M.D., has served as our chief medical officer since July 2015. Prior to this, Dr. Isaacs worked at Merck Research Laboratory, a division of Merck & Co., Inc., from 1997 to 2015. Between 2009 and 2015, Dr. Isaacs served as a vice president and therapeutic area head, leading the vaccine and infectious disease clinical development groups in global clinical development. Prior to that, he was an associate professor of infectious disease at the University of Mississippi Medical Center in Jackson, Mississippi. Dr. Isaacs completed a clinical and research fellowship in infectious diseases at the University of Texas Southwestern Medical Center in Dallas, Texas. Dr. Isaacs received his M.D. from the University of Auckland.

John Mueller, Ph.D., has served as our chief development officer since May 2015. Prior to this, Dr. Mueller served as senior project director at AstraZeneca AB from June 2011 to May 2015, where he led a global multidisciplinary team to advance zoliflodacin into a Phase 2 clinical trial. Prior to that, Dr. Mueller worked at Pfizer, Inc. and Alexion Pharmaceuticals, Inc. Dr. Mueller received his Ph.D. in Microbiology and Immunology from the Albany Medical College, and subsequently conducted post-doctoral studies at the Tufts Medical School as a National Institutes of Health fellow where he completed his bacterial genetics research training.

Ruben Tommasi, Ph.D., has served as our chief scientific officer since May 2015. Prior to this, Dr. Tommasi served as executive director of chemistry of the infection innovative medicines unit at AstraZeneca AB from May 2011 to May 2015. Before that, he led the infection chemistry unit at Novartis Institutes for Biomedical Research from December 2006 to April 2011. Prior to that, Dr. Tommasi worked at Novartis International AG. Dr. Tommasi received both his Ph.D. in Organic Chemistry and his Bachelors of Science from the State University of New York, Albany.

Non-Management Directors

Nicholas Galakatos, Ph.D., has served as chairman of our board of directors since March 2016. Dr. Galakatos is a managing director of Clarus, a health care and life sciences venture capital firm, which he co-founded in 2005. Dr. Galakatos has been a venture capital investor since 1992, initially at Venrock Associates and then at MPM Capital as general partner. Prior to that, he was vice president, new business, and a member of the management team at Millennium Pharmaceuticals, Inc., a biopharmaceutical company acquired by Takeda Pharmaceutical in May 2008, and was a founder of Millennium Predictive Medicine, Inc. and TransForm Pharmaceuticals, Inc., where he was the chairman and founding chief executive officer. Dr. Galakatos currently serves on the board of directors of Nanostring Technologies, Inc., Nuvelution Pharma, Inc. and Praxis Precision Medicines Inc. He has previously served as the lead director at Affymax Inc., and as a member of the boards of directors of Ophthotech Corporation, Portola Pharmaceuticals, Inc., Aveo Pharmaceuticals, Inc., and Catabasis Pharmaceuticals, Inc. Dr. Galakatos received a B.A. degree in Chemistry from Reed College, a Ph.D. degree in Organic Chemistry from the Massachusetts Institute of Technology, and performed postdoctoral studies in molecular biology at Harvard Medical School. We believe that Dr. Galakatos is qualified to serve on our board of directors because of his operating experience in the biopharmaceutical industry and his extensive experience as a venture capital investor and a director of public companies in the life sciences industry.

Heather Behanna, Ph.D., has served as a member of our board of directors since August 2017. Dr. Behanna has been a principal at Sofinnova Ventures since January 2017, focusing on biopharmaceutical investments. Prior to joining Sofinnova Ventures, Dr. Behanna was a senior vice president and biotechnology sell-side analyst at Wedbush Securities from August 2014 to December 2016, preceded by a role as an associate at JMP Securities from September 2010 to June 2014. Prior to this, Dr. Behanna worked in early stage drug discovery at the Astellas Research Institute and was also

an adjunct professor at the Feinberg School of Medicine at Northwestern University. Dr. Behanna received her Ph.D. in Chemistry from Northwestern University, an M.S. in Organic Chemistry from the Weizmann Institute of Science and her B.S. from Tufts University. We believe that Dr. Behanna is qualified to serve on our board of directors because of her extensive experience in the biopharmaceutical investment industry and her scientific background.

Thomas Dyrberg, M.D., D.M.Sc., has served as a member of our board of directors since March 2016. In December 2000, Dr. Dyrberg joined Novo Holdings A/S, a limited liability company wholly owned by the Novo Nordisk Foundation that is responsible for managing the Foundation's assets, where he serves as a managing partner of Novo Ventures. Prior to that, Dr. Dyrberg held positions at Novo Nordisk A/S. Dr. Dyrberg currently serves on the board of directors of Galera Therapeutics, Inc., Ophthotech Corporation and Nuvelution Pharma, Inc. Dr. Dyrberg received a D.M.Sc. and an M.D. from the University of Copenhagen. Dr. Dyrberg has held research positions at the Hagedorn Research Institute in Denmark and at the Scripps Research Institute in California. We believe that Dr. Dyrberg is qualified to serve on our board of directors because of his many years of industry experience, his extensive experience as a venture capital investor in the life sciences industry and his service on the board of directors of other life sciences companies.

David C. Hastings has served as a member of our board of directors since April 2018. Mr. Hastings served as the Senior Vice President and Chief Financial Officer of Unilife Corporation from February 2015 to June 2017 and as Unilife's Chief Accounting Officer and Treasurer from July 2016 to June 2017. From October 2003 to October 2014, Mr. Hastings served as Executive Vice President and Chief Financial Officer at Incyte Corporation. Mr. Hastings currently serves on the board of directors of Scynexis Inc. and VBL Therapeutics Ltd. Mr. Hastings received his B.A. in Economics from the University of Vermont. We believe that Mr. Hastings is qualified to serve on our board of directors because of his extensive financial experience, including experience as the chief financial officer of multiple publicly traded companies.

Robert Hopfner, Ph.D., has been a member of our board of directors since December 2017. Dr. Hopfner has served as a managing partner at Pivotal bioVenture Partners since October 2017. Prior to joining Pivotal, Dr. Hopfner was an investment partner and managing director at Bay City Capital, a venture capital firm, since August 2002. Before joining Bay City Capital, Dr. Hopfner worked as an associate in DuPont Pharmaceutical's business development and strategic planning group and as an analyst at Ag-West Biotech, a Western Canadian seed-stage biotech venture capital firm. Dr. Hopfner served on the board of directors of Hyperion Therapeutics, Inc., a public biopharmaceutical company, from 2010 to 2013. Dr. Hopfner holds a Ph.D. in Pharmacology and a B.S. in Pharmacy from the University of Saskatchewan and an MBA with specializations in Entrepreneurship, Finance and Strategy from the University of Chicago Booth School of Business. We believe that Dr. Hopfner is qualified to serve on our board of directors because of his experience in venture capital, particularly his experience investing in life sciences companies, and his medical background.

Gregory Norden has served as a member of our board of directors since October 2016. From 1989 to 2010, Mr. Norden held various senior positions at Wyeth/American Home Products, most recently as Wyeth's senior vice president and chief financial officer. Mr. Norden currently serves on the boards of directors of Nanostring Technologies, Inc., Royalty Pharma, Univision and Zoetis Inc. Mr. Norden previously served as a director of Welch Allyn, Inc. (acquired by Hill-Rom, Inc. in 2015), Lumara Health Inc. (acquired by AMAG Pharmaceuticals in 2014), and Human Genome Sciences Inc. (acquired by GlaxoSmithKline plc in 2012). Mr. Norden received a M.S. in Accounting from Long Island University—C.W. Post and a B.S. in Management/Economics from the State University of New York—Plattsburgh. We believe that Mr. Norden is qualified to serve on our board of directors because of his extensive financial and accounting expertise and experience at Wyeth and at Arthur Andersen & Company and his significant experience in the biopharmaceutical industry.

Heather Preston, M.D., has served as a member of our board of directors since August 2017. Dr. Preston has served as a managing partner at Pivotal bioVenture Partners and as a senior advisor at TPG Biotech, a biotechnology venture capital firm, since July 2018. Dr. Preston was previously a partner and managing director at TPG Biotech from 2005 to July 2018. Prior to joining TPG Biotech, Dr. Preston served for two years as a medical device and biotechnology venture capital investor at J.P. Morgan Partners, LLC, a private equity firm. Prior to that, she was an entrepreneur-in-residence at New Enterprise Associates, a venture capital firm, and was a leader of the pharmaceutical and medical products consulting practice at McKinsey & Co. Dr. Preston currently serves on the boards of directors of Alder BioPharmaceuticals, Inc., Otonomy, Inc. and a number of private companies. Dr. Preston served on the board of directors of Albireo Pharma, Inc. from 2008 to June 2018. Dr. Preston received her M.D. from the University of Oxford and a B.S. in Biochemistry from the University of London. We believe that Dr. Preston is qualified to serve on our board of directors because of her extensive experience in the biopharmaceutical investment industry and her scientific background.

Andrew J. Staples has served as a member of our board of directors since May 2015. Mr. Staples has served at AstraZeneca AB in a range of pharmaceutical and finance positions since 1997. He is a qualified Chartered Accountant and previously worked for PricewaterhouseCoopers LLP and Eli Lilly before joining AstraZeneca. Mr. Staples received a chemistry degree from The University of Sheffield. We believe that Mr. Staples is qualified to serve on our board of directors because of his extensive experience at AstraZeneca and his accounting background.

James N. Topper, M.D., Ph.D., has served as a member of our board of directors since March 2016. Since August 2003, he has been a partner with Frazier Healthcare Partners, a venture capital firm, currently holding the position of managing general partner of the life sciences team. Prior to this, Dr. Topper served as head of the cardiovascular research and development division at Millennium Pharmaceuticals, Inc. and prior to the merger of COR Therapeutics, Inc. and Millennium Pharmaceuticals in 2002, served as the vice president of biology at COR Therapeutics. He served on the faculties of Stanford Medical School and Harvard Medical School prior to joining COR Therapeutics. Dr. Topper currently serves on the board of directors of Allena Pharmaceuticals Inc. and AnaptysBio, Inc. Dr. Topper received a B.S. in Biology from the University of Michigan and an M.D. and a Ph.D. in Biophysics from the Stanford University School of Medicine. He did his postgraduate training in internal medicine and cardiovascular disease at the Brigham and Women's Hospital in Boston and is board certified in both disciplines. We believe that Dr. Topper is qualified to serve on our board of directors because of his management experience in our industry and knowledge of medical and scientific matters.

In the last ten years none of our directors were executive officers of a corporation that declared bankruptcy within two years of the director being an executive officer of that corporation other than Mr. Hastings, who was an executive officer of Unilife Corporation when it filed for voluntary bankruptcy in April 2017.

Board Composition

Our board of directors currently consists of 10 members. Our board of directors will consist of eight members following the resignation of Drs. Dyrberg and Hopfner upon the effectiveness of the registration statement of which this prospectus forms a part.

Our directors were elected to and currently serve on the board pursuant to a shareholders' agreement among us and all holders of our preferred stock. This agreement will terminate upon the completion of this offering, after which there will be no further contractual obligations regarding the election of our directors.

In accordance with our amended and restated certificate of incorporation, which will be in effect upon the completion of this offering, our board of directors will be divided into three classes, each of

which will consist, as nearly as possible, of one-third of the total number of directors constituting our entire board and which will serve staggered three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Our directors will be divided among the three classes as follows:

- Class I, which will consist of Heather Preston, Andrew J. Staples and James N. Topper, and their term will expire at our first annual meeting of stockholders to be held after the completion of this offering;
- Class II, which will consist of Gregory Norden and Heather Behanna, and their term will expire at our second annual meeting of stockholders to be held after the completion of this offering; and
- Class III, which will consist of Nicholas Galakatos, David Hastings and Manoussos Perros, and their term will expire at our third annual meeting of stockholders to be held after the completion of this offering.

Our amended and restated certificate of incorporation, which will be in effect upon the completion of this offering, will provide that the authorized number of directors may be changed only by resolution approved by a majority of our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control.

Director Independence

Our board of directors has undertaken a review of its composition, the composition of its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that all of our directors other than Dr. Perros have no relationships that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the applicable rules and regulations of the SEC and Nasdaq. Our board of directors has determined that Dr. Perros, by virtue of his position as our chief executive officer, is not independent under applicable rules and regulations of the SEC and Nasdaq. In making this determination, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our share capital held by each non-employee director.

Family Relationships

There are no family relationships among any of our directors or executive officers.

Committees of the Board of Directors

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which will have the composition and responsibilities described below upon completion of this offering. From time to time, the board may establish other committees to facilitate the oversight of our business.

Audit Committee

Effective upon completion of this offering, our audit committee will be composed of three directors, Heather Behanna, David Hastings and Andrew J. Staples, and our board of directors has determined that each of them is independent within the meaning of applicable Nasdaq listing requirements and the independence requirements contemplated by Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act. David Hastings is the chairman of the audit committee and our board of directors has determined that David Hastings is an "audit committee financial expert" as defined by SEC rules and regulations. Our board of directors has determined that the composition of our audit committee meets the criteria for independence under, and the functioning of our audit committee complies with, the applicable requirements of the Sarbanes-Oxley Act, applicable Nasdaq listing requirements and SEC rules and regulations. We intend to continue to evaluate the requirements applicable to us and we intend to comply with the future requirements to the extent that they become applicable to our audit committee. The principal duties and responsibilities of our audit committee include:

- appointing and retaining an independent registered public accounting firm to serve as independent auditor to audit our financial statements, overseeing the independent auditor's work and determining the independent auditor's compensation;
- approving in advance all audit services and non-audit services to be provided to us by our independent auditor;
- establishing procedures for the receipt, retention and treatment of complaints received by us regarding accounting, internal accounting controls, auditing or compliance matters, as well as for the confidential, anonymous submission by our employees of concerns regarding questionable accounting or auditing matters;
- reviewing and discussing with management and our independent auditor the results of the annual audit and the independent auditor's review of our quarterly financial statements; and
- conferring with management and our independent auditor about the scope, adequacy and effectiveness of our internal accounting controls, the objectivity of our financial reporting and our accounting policies and practices.

Compensation Committee

Effective upon completion of this offering, our compensation committee will be composed of three directors, Heather Preston, Gregory Norden and James N. Topper, each of whom is a non-employee member of our board of directors as defined in Rule 16b-3 under the Exchange Act. James N. Topper is the chairman of the compensation committee. Our board of directors has determined that the composition of our compensation committee satisfies the applicable independence requirements under, and the functioning of our compensation committee complies with the applicable requirements of, Nasdaq listing rules and SEC rules and regulations. We intend to continue to evaluate and intend to comply with all future requirements applicable to our compensation committee. The principal duties and responsibilities of our compensation committee include:

- establishing and approving, and making recommendations to the board of directors regarding, performance goals and objectives relevant to the compensation of our chief executive officer, evaluating the performance of our chief executive officer in light of those goals and objectives and setting, or recommending to the full board of directors for approval, the chief executive officer's compensation, including incentive-based and equity-based compensation, based on that evaluation;

- setting the compensation of our other executive officers, based in part on recommendations of the chief executive officer;
- exercising administrative authority under our stock plans and employee benefit plans;
- establishing policies and making recommendations to our board of directors regarding director compensation;
- reviewing and discussing with management the compensation discussion and analysis that we may be required from time to time to include in SEC filings; and
- preparing a compensation committee report on executive compensation as may be required from time to time to be included in our annual proxy statements or annual reports on Form 10-K filed with the SEC.

Nominating and Corporate Governance Committee

Effective upon completion of this offering, the nominating and corporate governance committee will be composed of three directors, Heather Behanna, Nicholas Galakatos and Gregory Norden. Nicholas Galakatos is the chairman of the nominating and corporate governance committee. Our board of directors has determined that the composition of our nominating and corporate governance committee satisfies the applicable independence requirements under, and the functioning of our nominating and corporate governance committee complies with the applicable requirements of, Nasdaq listing standards and SEC rules and regulations. We will continue to evaluate and will comply with all future requirements applicable to our nominating and corporate governance committee. The nominating and corporate governance committee's responsibilities include:

- assessing the need for new directors and identifying individuals qualified to become directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board's committees;
- assessing individual director performance, participation and qualifications;
- developing and recommending to the board corporate governance principles;
- monitoring the effectiveness of the board and the quality of the relationship between management and the board; and
- overseeing an annual evaluation of the board's performance.

Code of Business Conduct and Ethics for Employees, Executive Officers and Directors

Effective upon completion of this offering, we will adopt a Code of Business Conduct and Ethics, or the code of conduct, applicable to all of our employees, executive officers and directors. Following the completion of this offering, the code of conduct will be available on our website at *www.entasistx.com*. The nominating and corporate governance committee of our board of directors will be responsible for overseeing the code of conduct and must approve any waivers of the code of conduct for employees, executive officers and directors. We expect that any amendments to the code of conduct, or any waivers of its requirements for any executive officer or director, will be disclosed on our website.

Compensation Committee Interlocks and Insider Participation

None of our directors who currently serve as members of our compensation committee is, or has at any time during the past year been, one of our officers or employees. None of our executive officers currently serves, or in the past year has served, as a member of the board of directors or compensation

committee of any other entity that has one or more of its executive officers serving on our board of directors or compensation committee.

Limitation on Liability and Indemnification Matters

Our amended and restated certificate of incorporation, which will become effective immediately after the completion of this offering, and our amended and restated bylaws, which will become effective immediately prior to the completion of this offering, limits our directors' liability, and may indemnify our directors and officers to the fullest extent permitted under Delaware General Corporation Law, or the DGCL. The DGCL provides that directors of a corporation will not be personally liable for monetary damages for breach of their fiduciary duties as directors, except for liability for any:

- transaction from which the director derives an improper personal benefit;
- act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or redemption of shares; or
- breach of a director's duty of loyalty to the corporation or its stockholders.

These limitations of liability do not apply to liabilities arising under federal securities laws and do not affect the availability of equitable remedies such as injunctive relief or recession.

The DGCL and our amended and restated bylaws provide that we will, in certain situations, indemnify our directors and officers and may indemnify other employees and other agents, to the fullest extent permitted by law. Any indemnified person is also entitled, subject to certain limitations, to advancement, direct payment or reimbursement of reasonable expenses (including attorneys' fees and disbursements) in advance of the final disposition of the proceeding.

In addition, we have entered or will enter into indemnification agreements with our directors and officers. These indemnification agreements, among other things, require us to indemnify our directors and officers for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of their services as a director or officer, or any other company or enterprise to which the person provides services at our request.

We also maintain a directors' and officers' insurance policy pursuant to which our directors and officers are insured against liability for actions taken in their capacities as directors and officers.

We believe that these provisions in our amended and restated certificate of incorporation and amended and restated bylaws, these indemnification agreements and this insurance are necessary to attract and retain qualified persons as directors and officers.

Insofar as indemnification of liabilities arising under the Securities Act of 1933, as amended, or the Securities Act, may be permitted to our board of directors, executive officers, or persons controlling us pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

EXECUTIVE AND DIRECTOR COMPENSATION

Our named executive officers for the year ended December 31, 2017, which consist of our principal executive officer and our two other most highly compensated executive officers, are:

- Manoussos Perros, Ph.D., our President and Chief Executive Officer;
- Michael Gutch, Ph.D., our Chief Financial Officer and Chief Business Officer; and
- Robin Isaacs, M.D., our Chief Medical Officer.

Summary Compensation Table

The following table presents the compensation awarded to, earned by or paid to our named executive officers, during the years ended December 31, 2016 and 2017.

Name and Principal Position	Year	Salary ($)[1]	Bonus ($)[2]	Option Awards ($)[3]	All Other Compensation ($)	Total ($)
Manoussos Perros, Ph.D.	2017	429,867	190,794	720,767	8,100[4]	1,349,528
President and Chief Executive Officer	2016	413,333	194,688	145,035	7,950[4]	761,006
Michael Gutch, Ph.D.[6]	2017	228,750	93,782	192,464	67,654[5]	582,650
Chief Financial Officer and Chief Business Officer						
Robin Isaacs, M.D.	2017	383,760	152,812	103,722	8,100[4]	648,394
Chief Medical Officer	2016	372,000	160,233	37,835	119,765[7]	689,833

(1) Salary amounts represent actual amounts paid during the indicated year. See the subsection titled "—Narrative to Summary Compensation Table—Annual Base Salary" for a description of adjustments to base salaries made during the year.

(2) The amounts represent cash bonuses earned for the years indicated regardless of when paid.

(3) The amounts in this column represent the grant date fair value for option awards determined in accordance with ASC Topic 718, *Compensation—Stock Compensation*. Assumptions used in the calculation of these amounts are included in Note 8 to our consolidated financial statements included elsewhere in this prospectus, except that we assumed that the executive will perform the requisite service for the award to vest in full. These amounts do not reflect the actual economic value that will be realized by the named executive officer upon the vesting of the stock options, the exercise of the stock options or the sale of the common stock underlying such stock options.

(4) The amounts represent matching contributions made by us to the named executive officer's 401(k) plan account.

(5) This amount includes $61,354 for the reimbursement of moving costs and associated tax gross-up and $6,300 of matching contributions made by us to the named executive officer's 401(k) plan account.

(6) Dr. Gutch's employment with our company commenced on April 1, 2017.

(7) This amount includes $112,345 for the reimbursement of moving costs and associated tax gross-up and $7,420 of matching contributions made by us to the named executive officer's 401(k) plan account.

Narrative to Summary Compensation Table

We review compensation annually for all employees, including our executives. In setting executive base salaries and bonuses and granting equity incentive awards, we consider compensation for comparable positions in the market, the historical compensation levels of our executives, individual performance as compared to our expectations and objectives, our desire to motivate our employees to achieve short- and long-term results that are in the best interests of our stockholders, and a long-term commitment to our company. In addition, we have also engaged compensation consultants and take into consideration their assessments of our compensation.

The compensation committee of our board of directors has historically reviewed and made recommendations to our board of directors regarding our executives' compensation. Our compensation committee typically reviews and discusses management's proposed compensation with the chief executive officer for all executives other than the chief executive officer. Based on those discussions and its discretion, the compensation committee then recommends the compensation for each executive officer for approval by our board of directors. To date, our compensation committee has not adopted a peer group of companies for purposes of determining executive compensation.

Annual Base Salary

Base salaries for our executives are initially established through arm's length negotiation at the time the executive is hired, taking into account such executive's qualifications, experience, prior salary, the scope of his or her responsibilities and competitive market compensation paid by other companies for similar positions within the industry. Base salaries are reviewed annually in January by our compensation committee and approved by our board of directors in connection with our annual performance review process. Salaries may be adjusted from time to time to realign salaries with market levels after taking into account individual responsibilities, performance and experience. In making decisions regarding salary increases, we may also confer with a compensation consultant or draw upon the experience of members of our board of directors with other companies. Any approved salary increases are typically effective in March of the same year. The 2017 and 2018 base salaries of our named executive officers are as follows:

Name	2017 Base Salaries	2018 Base Salaries
Manoussos Perros, Ph.D.	$432,640	$449,946
Michael Gutch, Ph.D.	$305,000	$317,200
Robin Isaacs, M.D.	$385,632	$397,201

Annual Bonus

The offer letter agreement with each of our named executive officers provides that the officer may be eligible to earn an annual performance bonus of up to a target percentage of 35% (or in the case of our chief executive officer, 45%) of the executive's base salary. Our compensation committee reviews executive performance annually against pre-established goals, which are approved in January of each year for performance during that calendar year based on recommendations by our chief executive officer. Our compensation committee and board of directors may approve annual bonuses for our executive officers based on individual performance, company performance or as otherwise determined appropriate. Our board of directors determined that Drs. Perros, Gutch and Isaacs were entitled to 98%, 99% and 99%, respectively, of their 2017 target bonuses.

Long-Term Incentives

Our amended and restated stock incentive plan effective as of May 11, 2015 and as amended from time to time, or our 2015 Plan, authorizes us to make grants to eligible recipients of stock options qualifying as incentive stock options, non-qualified stock options, restricted share awards, restricted share units and other share-based awards. Upon the consummation of the corporate reorganization, we assumed the 2015 Plan from our predecessor, Entasis Therapeutics Limited.

We typically grant stock options at the start of employment to each executive and our other employees. We do not currently maintain a practice of granting additional equity on an annual basis, but do provide additional targeted grants in appropriate circumstances.

We award stock options on the date our board of directors approves the grant. We set the option exercise price and grant date fair value based on our per-share valuation on the date of grant.

In June 2017, our board of directors awarded stock options to Dr. Gutch upon commencement of his employment with us. Dr. Gutch received an option to purchase 41,069 shares of our common stock with an exercise price of $3.74 per share. Of the shares underlying this option, 25% vested on April 1, 2018, and the remaining shares vest in 36 equal monthly installments thereafter. In November 2017, our board of directors awarded stock options to each of our named executive officers. Drs. Perros, Gutch and Isaacs received an option to purchase 183,013 shares of our common stock, 25,092 shares of our common stock and 26,336 shares of our common stock, respectively. Each of these options has an exercise price of $3.11 per share. Of the shares underlying each of these options, 25% vests on August 25, 2018, and the remaining shares vest in 36 equal monthly installments thereafter.

In October 2016, our board of directors awarded stock options to each of our named executive officers. Drs. Perros and Isaacs received options to purchase 69,970 shares of our common stock and 18,253 shares of our common stock, respectively. Each of these options has an exercise price of $3.74 per share. Of the shares underlying each of these options, 25% vested on March 29, 2017, and the remaining shares vest in 36 equal monthly installments thereafter.

Employment Arrangements and Potential Payments upon Termination of Employment or Change of Control

We currently have offer letter agreements with each of our named executive officers, and in September 2018, we entered into employment agreements with each of our named executive officers that become effective on the date of effectiveness of the registration statement of which this prospectus is a part. Furthermore, each of our named executive officers has executed a form of our standard confidentiality and proprietary rights agreement. The key terms of our employment arrangements with our named executive officers, including potential payments upon termination or change in control, are described below.

Agreement with Dr. Perros

We entered into an offer letter with Manoussos Perros, our president and chief executive officer, dated May 11, 2015, which set forth the initial terms and conditions of his employment with us. On August 28, 2017, we amended the terms of our offer letter with Dr. Perros. Pursuant to the offer letter, Dr. Perros is entitled to a base salary of $449,946 per year, as may be adjusted from time to time in accordance with our normal business practices. Dr. Perros is also eligible to receive an annual target bonus of up to 45% of his base salary. In connection with the execution of his offer letter, Dr. Perros also received a one-time, lump-sum retention bonus of $252,489. The offer letter also provided for the grant of an option to purchase a number of shares of our common stock equal to 4.6% of our outstanding shares on a fully diluted basis at the time of grant pursuant to our 2015 Plan, which was equal to 87,462 shares of our common stock and was granted to Dr. Perros on August 11, 2015. Dr. Perros' employment is at will and may be terminated by him or by us at any time, with or without cause.

In September 2018, we entered into an employment agreement with Dr. Perros that becomes effective on the date of effectiveness of the registration statement of which this prospectus is a part, which sets forth the revised terms of Dr. Perros' employment with us. Pursuant to Dr. Perros' employment agreement, Dr. Perros will receive an initial annual base salary of $449,946, as may be adjusted from time to time in accordance with our normal business practices, is eligible to receive an annual performance bonus with a target of 45% of his then-current base salary, as determined by our board of directors, and reimbursement for expenses. His employment agreement does not have a specified term and his employment may be terminated by us or by Dr. Perros at any time, with or without cause. Dr. Perros' employment agreement will amend and replace the terms of his employment

contained in his offer letter. Dr. Perros is additionally eligible for certain severance and change in control benefits pursuant to his employment agreement, the terms of which are described below under "—Potential Payments and Benefits upon Termination or Change of Control."

Agreement with Dr. Gutch

We entered into an offer letter with Michael Gutch, our chief business officer and chief financial officer, dated January 4, 2017, which set forth the initial terms and conditions of his employment with us. On August 28, 2017, we amended the terms of our offer letter with Dr. Gutch. Pursuant to the offer letter, Dr. Gutch is entitled to a base salary of $317,200 per year, as may be adjusted from time to time in accordance with our normal business practices. Dr. Gutch is also eligible to receive an annual target bonus with a target of 35% of his then-current base salary. The offer letter provides that he was eligible to be reimbursed for expenses of up to $100,000 in connection with the relocation of his principal residence to Massachusetts during the period beginning on his start date and ending on December 31, 2018, to be paid within 60 days following his relocation, and an additional payment to cover any taxes due on the relocation reimbursements. Dr. Gutch is required to repay those amount if his employment is terminated by the Company for cause or by him without good reason prior to the second anniversary of this relocation. The offer letter also provided for the grant of an option to purchase a number of shares of our common stock equal to 1.162% of our outstanding shares on a fully diluted basis at the time of grant pursuant to our 2015 Plan, which was equal to 41,069 shares of our common stock and was granted to Dr. Gutch on June 1, 2017. Dr. Gutch's employment is at will and may be terminated by him or by us at any time, with or without cause.

In September 2018, we entered into an employment agreement with Dr. Gutch that becomes effective on the date of effectiveness of the registration statement of which this prospectus is a part, which sets forth the revised terms of Dr. Gutch's employment with us. Pursuant to Dr. Gutch's employment agreement, Dr. Gutch will receive an initial annual base salary of $317,200, as may be adjusted from time to time in accordance with our normal business practices, is eligible to receive an annual performance bonus with a target of 35% of his then-current base salary, as determined by our board of directors, and reimbursement for expenses. His employment agreement does not have a specified term and his employment may be terminated by us or by Dr. Gutch at any time, with or without cause. Dr. Gutch's employment agreement will amend and replace the terms of his employment contained in his offer letter. Dr. Gutch is additionally eligible for certain severance and change in control benefits pursuant to his employment agreement, the terms of which are described below under "—Potential Payments and Benefits upon Termination or Change of Control."

Agreement with Dr. Isaacs

We entered into an offer letter with Robin Isaacs, our chief medical officer, dated June 3, 2015, which set forth the initial terms and conditions of his employment with us. On August 28, 2017, we amended the terms of our offer letter with Dr. Isaacs. Pursuant to the offer letter, Dr. Isaacs is entitled to a base salary of $397,201 per year, as may be adjusted from time to time in accordance with our normal business practices. Dr. Isaacs is also eligible to receive an annual target bonus of up to 35% of his base salary. In connection with the execution of his offer letter, Dr. Isaacs also received a sign-on bonus of $45,000, $25,000 of which was paid on the first anniversary of his start date and the remainder on the second anniversary of his start date. The offer letter provides that he was eligible to be reimbursed for expenses of up to $100,000 in connection with the relocation of his principal residence to Massachusetts within 12 months following his start date, to be paid within 60 days following his relocation, and an additional payment to cover any taxes due on the relocation reimbursements. The offer letter also provided for the grant of an option to purchase a number of shares of our common stock equal to 1.2% of our outstanding shares on a fully diluted basis at the time of grant pursuant to our 2015 Plan, which was equal to 22,816 shares of our common stock and was granted to Dr. Isaacs

on August 11, 2015. Dr. Isaacs' employment is at will and may be terminated by him or by us at any time, with or without cause.

In September 2018, we entered into a new employment agreement with Dr. Isaacs that becomes effective on the date of effectiveness of the registration statement of which this prospectus is a part, which sets forth the revised terms of Dr. Isaacs' employment with us. Pursuant to Dr. Isaacs' employment agreement, Dr. Isaacs will receive an initial annual base salary of $397,201, as may be adjusted from time to time in accordance with our normal business practices, is eligible to receive an annual performance bonus with a target of 35% of his then-current base salary, as determined by our board of directors, and reimbursement for expenses. His employment agreement does not have a specified term and his employment may be terminated by us or by Dr. Isaacs at any time, with or without cause. Dr. Isaac's employment agreement will amend and replace the terms of his employment contained in his offer letter. Dr. Isaacs is additionally eligible for certain severance and change in control benefits pursuant to his employment agreement, the terms of which are described below under "—Potential Payments and Benefits upon Termination or Change of Control."

Potential Payments and Benefits upon Termination or Change of Control

Each of the amended offer letter agreements with our named executive officers provides that if we terminate the employment of the named executive officer for any reason other than for cause, or if such executive officer resigns his position with us for good reason, he would be entitled to receive the following severance benefits for the lesser of (i) six (or in the case of Dr. Perros, 12) months following his termination date and (ii) the date on which he commences full-time employment with another employer or entity:

- continued payment of his then-current base salary in accordance with our payroll practices; and
- provided the executive officer is eligible for and timely elects to continue receiving group medical insurance, we will continue to pay the share of the health insurance premiums that we otherwise pay for similarly situated employees who receive the same type of coverage.

Alternatively, if such termination or resignation occurs within 18 months after a change of control, the named executive officer is instead entitled to a lump-sum payment equal to 12 (or in the case of Dr. Perros, 24) months of his then current base salary, acceleration of vesting of the entire unvested portion of the outstanding stock options granted in connection with the offer letter and continued payment of health insurance premiums for 12 (or in the case of Dr. Perros, 24) months.

Each amended offer letter agreement provides that termination in connection with the named executive officer's death or disability or a deemed liquidation event, as defined in our articles of association, in which one or more holders of preference shares is not repaid its total investment amount will not constitute a termination without cause or for good reason for purposes of an executive officer being eligible to receive any severance or change in control severance benefits. Payment of any of the above-described severance benefits is conditioned on the executive officer's delivery and non-revocation of a severance and release of claims agreement, which will include a general release of claims and confidentiality, non-disparagement and cooperation provisions in our favor, within 60 days after such executive officer's termination.

Each of the employment agreements with our named executive officers that replace the offer letters as of the date of effectiveness of the registration statement of which this prospectus is a part provides that if we terminate the employment of the named executive officer for any reason other than for cause, or if such executive officer resigns his position with us for good reason, he would be eligible to receive the following severance benefits:

- 12 (or in the case of Dr. Perros, 18) months of his then-current base salary, paid in installments on our regular payroll dates following his termination date; and

- provided the executive officer is participating in our group health insurance as of the date of termination and timely elects to continue receiving coverage, we will continue to pay premiums necessary to continue executive and executive's covered dependents' health insurance coverage in effect on the termination date for the lesser of:
  - 12 (or in the case of Dr. Perros, 18) months;
  - the date on which he becomes eligible for health insurance coverage in connection with new employment or self-employment; or
  - the date he ceases to be eligible for continuation coverage for any reason, including plan termination.

Alternatively, if such termination or resignation occurs on or within 18 months after a change of control, the named executive officer is instead eligible for:

- a lump-sum payment equal to 12 (or in the case of Dr. Perros, 18) months of his then-current base salary;
- a lump-sum payment equal to one (or in the case of Dr. Perros, one and one half) times his target bonus for the year in which his employment terminates;
- provided the executive officer is eligible for and timely elects to continue receiving group health insurance, we will continue to pay premiums necessary to continue executive and executive's covered dependents' health insurance coverage in effect on the termination date for the lesser of:
  - 12 (or in the case of Dr. Perros, 18) months;
  - the date on which he becomes eligible for health insurance coverage in connection with new employment or self-employment; or
  - the date he ceases to be eligible for continuation coverage for any reason, including plan termination; and
- acceleration of vesting of the entire unvested portion of the outstanding stock options and other stock awards 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.

Each employment agreement provides that the named executive officer's death or disability terminates the employment relationship and executive's legal representatives will not receive severance benefits. Payment of any of the above-described severance benefits is conditioned on the executive officer's delivery and non-revocation of a severance and release of claims agreement, which will include a general release of claims in our favor, within the time period provided in such agreement, which will be no later than 60 days after such executive officer's termination.

For purposes of the new employment agreements:

- "cause" generally means (i) a material breach of the employment agreement or any other written agreement between the executive and us; (ii) gross negligence or gross misconduct in the performance of the executive's duties; (iii) the commission of any act or omission constituting dishonesty or fraud that is injurious to us or any affiliate thereof; (iv) any conduct which constitutes a felony under applicable law; (v) conduct by the executive which demonstrates gross unfitness to serve; (vi) failure to attempt in good faith to implement a clear, reasonable and legal directive of our board of directors or any board committee; or (vii) breach of a fiduciary duty.

- "good reason" means the occurrence, without the named executive's consent, of any of the following events: (i) any material diminution of the executive's authority, duties or responsibilities; (ii) a material (greater than 10%) reduction by us of the executive's base salary except in the case of across-the-board salary reductions based on our financial performance similarly affecting all or substantially all of our similarly-situated employees; (iii) a relocation of the executive's place of employment to a location in excess of 50 miles from our current principal place of employment; or (iv) any material breach of the employment agreement by us; *provided, however*, that it will only be deemed good reason if (1) we have not previously notified the executive of our intention to terminate his employment; (2) we have been given written notice from the executive within 90 days following the first occurrence of a condition that the executive considers to constitute good reason (with such notice including a description of the condition); (3) we fail to remedy such condition within 30 days following such written notice; and (4) the executive resigns from employment with us effective not later than 30 days after the end of our cure period. Notwithstanding the foregoing, any actions taken by us to accommodate a disability of the 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 the employment agreement.

Outstanding Equity Awards

The following table provides information about outstanding share awards held by each of our named executive officers at December 31, 2017. All of these share awards were granted pursuant to our 2015 Plan.

	Option Awards			
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date
Manoussos Perros, Ph.D.	56,486	30,976[1]	4.98	08/11/2025
	30,612	39,358[2]	3.74	10/21/2026
	—	183,013[3]	3.11	11/22/2027
Michael Gutch, Ph.D.	—	41,069[4]	3.74	06/01/2027
	—	25,092[3]	3.11	11/22/2027
Robin Isaacs, M.D.	13,785	9,031[5]	4.98	08/11/2025
	7,986	10,267[2]	3.74	10/21/2026
	—	26,336[3]	3.11	11/22/2027

(1) Of the shares underlying the option, 25% vested on May 13, 2016, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date. The option is subject to accelerated vesting upon a qualifying termination of the executive's employment with us, as described under "Executive Compensation—Employment Arrangements and Potential Payments upon Termination of Employment or Change of Control."

(2) Of the shares underlying the option, 25% vested on March 29, 2017, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date.

(3) Of the shares underlying the option, 25% vest on August 25, 2018, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date.

(4) Of the shares underlying the option, 25% vest on April 1, 2018, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date. The option is subject to accelerated vesting upon a qualifying termination of the executive's employment with us, as described under "Executive Compensation—Employment Arrangements and Potential Payments upon Termination of Employment or Change of Control."

(5) Of the shares underlying the option, 25% vested on July 1, 2016, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date. The option is subject to accelerated vesting upon a qualifying termination of the executive's employment with us, as described under "Executive Compensation—Employment Arrangements and Potential Payments upon Termination of Employment or Change of Control."

Pension Benefits

Our named executive officers did not participate in, or otherwise receive any benefits under, any defined benefit pension plan sponsored by us during 2017.

Nonqualified Deferred Compensation

Our named executive officers did not participate in, or otherwise receive any benefits under, any nonqualified deferred compensation plan sponsored by us during 2017.

Health and Welfare Benefits

All of our current named executive officers are eligible to participate in our employee benefit plans, including our medical, dental and vision insurance plans, in each case on the same basis as all of our other employees.

401(k) Plan

We maintain a defined contribution retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees may defer eligible compensation on a pre-tax basis, up to the statutorily prescribed annual limits on contributions under the Internal Revenue Code of 1986, as amended, or the Code. Contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participants' directions. Employees are immediately and fully vested in their contributions. The 401(k) plan is intended to be qualified under Section 401(a) of the Code with the 401(k) plan's related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to the 401(k) plan and earnings on those contributions are not taxable to the employees until distributed from the 401(k) plan. Pursuant to our 401(k) plan, during 2016 and 2017, we made 50% matching contributions on up to 6% of an employee's eligible compensation.

Equity Incentive Plans

2018 Equity Incentive Plan

Our board of directors adopted and our stockholders approved the 2018 Plan in September 2018. We do not expect to issue equity awards under our 2018 Plan until after the completion of this offering. No awards have been granted and no common stock has been issued under our 2018 Plan. Our 2018 Plan will provide for the grant of stock options qualifying as incentive stock options, or ISOs, within the meaning of Section 422 of the Code, to our employees and our parent and subsidiary corporations' employees, and for the grant of nonstatutory stock options, or NSOs, restricted stock awards, restricted stock unit awards, stock appreciation rights, performance stock awards and other forms of stock compensation to our employees, consultants and directors. Our 2018 Plan will also provide for the grant of performance cash awards to our employees, consultants and directors. Once the 2018 Plan is effective, no further grants will be made under the 2015 Plan.

Authorized Shares

The number of shares of our common stock initially reserved for issuance under our 2018 Plan is 2,350,000, which is the sum of (i) 1,095,864 shares of our common stock, (ii) the number of shares

remaining available for issuance under our 2015 Plan when the 2018 Plan becomes effective and (iii) the number of shares of our common stock subject to outstanding awards under our 2015 Plan when the 2018 Plan becomes effective that thereafter expire or are forfeited, canceled, withheld to satisfy tax withholding or to purchase or exercise an award, repurchased by us or are otherwise terminated. The number of shares of our common stock reserved for issuance under our 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 our common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by our 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.

Shares issued under our 2018 Plan may be authorized but unissued or reacquired shares of our common stock. Shares subject to stock awards granted under our 2018 Plan that expire or terminate without being exercised in full, or that are paid out in cash rather than in shares, will not reduce the number of shares available for issuance under our 2018 Plan. Additionally, shares issued pursuant to stock awards under our 2018 Plan that we repurchase or that are forfeited, as well as shares reacquired by us as consideration for the exercise or purchase price of a stock award or to satisfy tax withholding obligations related to a stock award, will become available for future grant under our 2018 Plan.

Administration

Our board of directors, or a duly authorized committee thereof, has the authority to administer our 2018 Plan. Our board of directors has delegated its authority to administer our 2018 Plan to our compensation committee under the terms of the compensation committee's charter. Our board of directors may also delegate to one or more of our officers the authority to (i) designate employees other than officers to receive specified stock awards and (ii) determine the number of shares of our common stock to be subject to such stock awards. Subject to the terms of our 2018 Plan, the administrator has the authority to determine the terms of awards, including recipients, the exercise price or strike price of stock awards, if any, the number of shares subject to each stock award, the fair market value of a share of our common stock, the vesting schedule applicable to the awards, together with any vesting acceleration, the form of consideration, if any, payable upon exercise or settlement of the stock award and the terms and conditions of the award agreements for use under our 2018 Plan.

The administrator has the power to modify outstanding awards under our 2018 Plan. Subject to the terms of our 2018 Plan, the administrator has the authority to reprice any outstanding option or stock award, cancel and re-grant any outstanding option or stock award in exchange for new stock awards, cash or other consideration, or take any other action that is treated as a repricing under generally accepted accounting principles, with the consent of any adversely affected participant.

Limitation on Grants to Non-Employee Directors

The maximum number of shares of our common stock subject to awards granted under our 2018 Plan or otherwise during a single calendar year to any of our non-employee directors, taken together with any cash fees paid by us to such non-employee director during the calendar year for serving on our board, will not exceed $500,000 in total value (the value of any such stock awards to be based on their grant date fair market value for financial reporting purposes), or, with respect to the calendar year in which a non-employee director is first appointed or elected to our board, $800,000.

Corporate Transactions

Our 2018 Plan provides that in the event of a specified corporate transaction, including without limitation a consolidation, merger, or similar transaction involving our company, the sale or other disposition of all or substantially all of the assets of our company or the consolidated assets of our

company and our subsidiaries, or a sale or disposition of more than 50% of the outstanding capital stock of our company, the administrator will determine how to treat each outstanding stock award. The administrator may:

- arrange for the assumption, continuation or substitution of a stock award by a successor corporation;
- arrange for the assignment of any reacquisition or repurchase rights held by us to a successor corporation;
- accelerate the vesting of the stock award and provide for its termination prior to the effective time of the corporate transaction;
- arrange for the lapse, in whole or in part, of any reacquisition or repurchase right held by us;
- cancel the stock award prior to the transaction in exchange for such cash consideration, if any, that the administrator in its discretion determines to be appropriate; or
- make a payment in a form determined by the administrator equal to the excess of the value of the property the participant would have received upon exercise of the stock award immediately prior to the transaction over the exercise price payable in connection with the stock award.

The administrator is not obligated to treat all stock awards or portions of stock awards, even those that are of the same type, in the same manner. The administrator may take different actions with respect to the vested and unvested portions of a stock award.

Change in Control

The administrator may provide, in an individual award agreement or in any other written agreement between us and the participant, that the stock award will be subject to additional acceleration of vesting and exercisability in the event of a change in control (as defined in the 2018 Plan). In the absence of such a provision, no such acceleration of the stock award will occur.

Amendment or Termination

Our board has the authority to amend, suspend, or terminate our 2018 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. No ISOs may be granted after the tenth anniversary of the date our board of directors adopts our 2018 Plan.

2015 Stock Incentive Plan

The board of directors of our predecessor originally adopted and its stockholders approved the 2015 Plan in May 2015. The 2015 Plan was amended in September 2015, and was subsequently amended and restated in March 2016, August 2017 and December 2017. We assumed the 2015 Plan upon completion of the corporate reorganization in April 2018. All references herein to our 2015 Plan, shall be deemed to refer to our 2015 Plan as amended and restated, unless the context otherwise requires. After the effective date of the 2018 Plan, no additional stock awards will be granted under the 2015 Plan.

Our 2015 Plan provides for the grant of ISOs, NSOs, stock appreciation rights, restricted stock awards, restricted stock unit awards, phantom stock and dividend equivalent rights, or collectively, stock awards. ISOs may be granted only to our employees, including our officers, and the employees of our affiliates. All other stock awards may be granted to our employees, including our officers, directors, consultants and advisors and those of our affiliates.

Authorized Shares

The aggregate number of shares able to be issued pursuant to stock awards under our 2015 Plan is 1,267,680 shares of our common stock. As of June 30, 2018, options to purchase 1,168,938 shares of our common stock, at exercise prices ranging from $3.11 to $6.85 per share, or a weighted-average exercise price of $4.70 per share, were outstanding under our 2015 Plan.

Shares subject to stock awards granted under our 2015 Plan that are forfeited, expire or terminate without delivery of shares subject to the award, or that are paid out in cash rather than in shares, will again be available for issuance under our 2015 Plan.

Plan Administration

Our board of directors administers our 2015 Plan. However, our board of directors may delegate its powers under the 2015 Plan to a committee established by the board, and following this offering, the compensation committee of our board of directors will administer our 2015 Plan. Our board of directors has full authority and discretion to take any actions it deems necessary or advisable for the administration of our 2015 Plan. Subject to the terms of our 2015 Plan, our board of directors has the authority to determine the terms of stock awards, including:

- recipients;
- the price at which options shall be granted;
- the type of option to be granted;
- the number of shares subject to each stock award; and
- the form and terms and conditions of each stock award.

Subject to the terms of our 2015 Plan, our board of directors also generally has the authority to amend awards, subject to the award recipient's consent if the amendment is not favorable to the participant, except in connection with a change of control.

Stock Options

ISOs and NSOs are granted pursuant to option documents adopted by the plan administrator. The plan administrator determines the exercise price for stock options, within the terms and conditions of our 2015 Plan, provided that the exercise price of a stock option generally cannot be less than the greater of 100% of the fair market value of our common stock on the date of grant or the par value of shares over which the option is granted. Options granted under our 2015 Plan vest at the rate specified in the option document as determined by the plan administrator, and expire at the time determined by the administrator, but in no event more than 10 years after they are granted, or earlier if the participant's service terminates.

Changes to Capital Structure

In the event that there is a specified type of change in our capital structure, such as a stock split or recapitalization, appropriate adjustments will be made to the class and maximum number of shares reserved for issuance under our 2015 Plan, the maximum number of shares that may be issued upon the exercise of options to any individual during any one calendar year, and the class and number of shares and exercise price of outstanding stock awards.

Change in Control

Our 2015 Plan provides that in the event of a change in control transaction (as defined in the 2015 Plan) the plan administrator may take whatever action with respect to options and stock awards

outstanding as it deems necessary or desirable, including, without limitation, accelerating the vesting, expiration or termination date or the date of exercisability in any option documents, or removing any restrictions from or imposing any additional restrictions on any outstanding awards.

Transferability

A participant generally may not transfer stock awards under our 2015 Plan other than by will, the laws of descent and distribution, or as otherwise provided under our 2015 Plan.

Amendment or Termination

Our board of directors has the authority to amend our 2015 Plan, provided that no amendment may make any changes as to which stockholder approval is required without obtaining such approval, or adversely affect the existing rights of any participant without such participant's consent. Certain material amendments also require the approval of our stockholders. No option or award may be granted after the tenth anniversary of the effective date of the 2015 Plan, which was May 11, 2015. No option or awards may be granted under our 2015 Plan after it is terminated.

2018 Employee Stock Purchase Plan

Our board of directors adopted and our stockholders approved the ESPP in September 2018. The ESPP will become effective upon completion of this offering. The purpose of the ESPP is to secure the services of new employees, to retain the services of existing employees and to provide incentives for such individuals to exert maximum efforts toward our success and that of our affiliates. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Code.

Share Reserve

Following this offering, the ESPP will authorize the issuance of 140,000 shares of our common stock pursuant to purchase rights granted to our employees or to employees of any of our designated affiliates. The number of shares of our common stock reserved for issuance will automatically increase on January 1 of each calendar year, from January 1, 2019 (assuming the ESPP becomes effective in 2018) through January 1, 2028, by the lesser of (i) 1% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, and (ii) 250,000 shares; provided, that prior to the date of any such increase, our board of directors may determine that such increase will be less than the amount set forth in clauses (i) and (ii). If purchase rights granted under the ESPP terminate without having been exercised, the shares of our common stock not purchased under such purchase rights will again become available for issuance under the ESPP.

Administration

Our board of directors intends to delegate concurrent authority to administer the ESPP to our compensation committee. The ESPP is implemented through a series of offerings under which eligible employees are granted purchase rights to purchase shares of our common stock on specified dates during such offerings. Under the ESPP, we may specify offerings with durations of not more than 27 months, and may specify shorter purchase periods within each offering. Each offering will have one or more purchase dates on which shares of our common stock will be purchased for employees participating in the offering. An offering under the ESPP may be terminated under certain circumstances.

Payroll Deductions

Generally, all regular employees, including executive officers, employed by us or by any of our designated affiliates, may participate in the ESPP and may contribute, normally through payroll deductions, up to 15% of their earnings (as defined in the ESPP) for the purchase of our common stock under the ESPP. Unless otherwise determined by our board of directors, common stock will be purchased for the accounts of employees participating in the ESPP at a price per share equal to the lower of (i) 85% of the fair market value of a share of our common stock on the first trading date of an offering or (ii) 85% of the fair market value of a share of our common stock on the date of purchase.

Limitations

Employees may have to satisfy one or more of the following service requirements before participating in the ESPP, as determined by our board of directors, including: (i) being customarily employed for more than 20 hours per week; (ii) being customarily employed for more than five months per calendar year; or (iii) continuous employment with us or one of our affiliates for a period of time (not to exceed two years). No employee may purchase shares under the ESPP at a rate in excess of $25,000 worth of our common stock based on the fair market value per share of our common stock at the beginning of an offering for each year such a purchase right is outstanding. Finally, no employee will be eligible for the grant of any purchase rights under the ESPP if immediately after such rights are granted, such employee has voting power over 5% or more of our outstanding capital stock measured by vote or value pursuant to Section 424(d) of the Code.

Changes to Capital Structure

In the event that there occurs a change in our capital structure through such actions as a stock split, merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, large nonrecurring cash dividend, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or similar transaction, the board of directors will make appropriate adjustments to (i) the number of shares reserved under the ESPP, (ii) the maximum number of shares by which the share reserve may increase automatically each year, (iii) the number of shares and purchase price applicable to all outstanding offerings and purchase rights and (iv) the number of shares that are subject to purchase limits under ongoing offerings.

Corporate Transactions

In the event of certain significant corporate transactions, including (i) a sale of all or substantially all of our assets, (ii) the sale or disposition of more than 50% of our outstanding securities, (iii) the consummation of a merger or consolidation where we do not survive the transactions and (iv) the consummation of a merger or consolidation where we do survive the transaction but the shares of our common stock outstanding immediately prior to such transaction are converted or exchanged into other property by virtue of the transaction, any then-outstanding rights to purchase our stock under the ESPP may be assumed, continued or substituted for by any surviving or acquiring entity (or its parent company). If the surviving or acquiring entity (or its parent company) elects not to assume, continue or substitute for such purchase rights, then the participants' accumulated payroll contributions will be used to purchase shares of our common stock within 10 business days prior to such corporate transaction, and such purchase rights will terminate immediately.

Amendments or Termination

Our board of directors has the authority to amend or terminate our ESPP, provided that except in certain circumstances such amendment or termination may not materially impair any outstanding

purchase rights without the holder's consent. We will obtain stockholder approval of any amendment to our ESPP, as required by applicable law or listing requirements.

Non-Employee Director Compensation

We have not historically had a formal compensation policy with respect to service on our board of directors, but we have reimbursed our non-employee directors for direct expenses incurred in connection with attending meetings of our board of directors or its committees, and occasionally granted stock options.

In September 2018, our board of directors approved a non-employee director compensation policy that will be effective upon the effectiveness of the registration statement of which this prospectus is a part. Under this policy, we will pay each of our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chairperson of each committee will receive a higher retainer for such service. These retainers are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on our board of directors or the applicable committee. No retainers will be paid in respect of any period prior to the completion of this offering. The retainers to be paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

Position	Annual Service Retainer	Chairperson Additional Annual Retainer
Board of directors	$35,000	$25,000
Audit committee	7,500	7,500
Compensation committee	5,500	5,500
Nominating and corporate governance committee	4,000	4,000

In addition, under our non-employee director compensation policy, each non-employee director elected to our board of directors after the completion of this offering will receive an option to purchase 13,000 shares of our common stock. The shares subject to each such stock option will vest annually over a three-year period, subject to the director's continued service as a director. Further, on the date of each annual meeting of stockholders held after the completion of this offering, each non-employee director that continues to serve as a non-employee member on our board of directors will receive an option to purchase 6,500 shares of our common stock. The shares subject to each such stock option will vest in full on the date that is 12 months after the grant date, subject to the director's continued service as a director. The exercise price per share of these options will equal the fair market value of our common stock on the date of grant.

This policy is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders.

Director Compensation Table

None of our non-employee directors received compensation for service on our board of directors during the year ended December 31, 2017, except for Mr. Norden, which compensation is set forth in the following table. Dr. Perros also served on our board of directors, but did not receive any additional compensation for his service as a director and therefore is not included in the table below. The

compensation for Dr. Perros as an executive officer is set forth above under the subsection titled "—Summary Compensation Table."

Name	Option Awards[1]
Gregory Norden	$20,144[2]

(1) This column reflects the aggregate grant date fair value of the option awards granted during fiscal year 2017 computed in accordance with ASC 718. Assumptions used in the calculation of these amounts are included in the notes to our consolidated financial statements included elsewhere in this prospectus, except that we assumed that the director will perform the requisite service for the award to vest in full. These amounts do not reflect the actual economic value that will be realized by our non-employee directors upon the vesting of the stock options, the exercise of the stock options or the sale of the shares underlying such stock options.

(2) Represents an option to purchase 5,114 shares of common stock at an exercise price of $3.11 per share. Of the shares underlying this option, 25% will vest on August 25, 2018, and the remaining shares vest in 36 equal monthly installments thereafter.

(3) The following table provides information regarding equity awards granted to our non-employee directors that were outstanding as of December 31, 2017:

Name	Option Awards Outstanding at Year-End
Gregory Norden	14,762

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from them. The director or officer may amend a Rule 10b5-1 plan in some circumstances and may terminate a plan at any time. Our directors and executive officers also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material nonpublic information subject to compliance with the terms of our insider trading policy. Prior to 180 days after the date of this offering, subject to early termination, the sale of any shares under such plan would be prohibited by the lock-up agreement that the director or officer has entered into with the underwriters for this offering.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of transactions since our inception on March 6, 2015 to which we have been a participant in which the amount involved exceeded or will exceed $120,000, and in which any of our directors, executive officers or holders of more than 5% of our share capital, or any members of their immediate family, had or will have a direct or indirect material interest, other than compensation arrangements which are described under the section titled "Executive Compensation." Pursuant to our corporate reorganization, all shares issued in connection with the transactions discussed below have been exchanged for the same number and classes of newly issued shares of preferred and common stock of Entasis Therapeutics Holdings Inc. See "Corporate Reorganization."

Participation in this Offering

Certain of our existing stockholders and their affiliated entities have indicated an interest in purchasing up to an aggregate of $50.0 million of shares of our common stock in this offering at the initial public offering price per share. Based on an assumed initial public offering price of $17.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, these entities would purchase up to an aggregate of 2,941,176 shares in this offering based on these indications of interest. However, because indications of interest are not binding agreements or commitments to purchase, these entities may determine to purchase fewer shares than they indicate an interest in purchasing or not to purchase any shares in this offering. It is also possible that these entities could indicate an interest in purchasing more of our shares. In addition, the underwriters could determine to sell fewer shares to any of these entities than the entities indicate an interest in purchasing or not to sell any shares to these entities.

Transactions with AstraZeneca AB

In connection with our spin-out from AstraZeneca AB, or AstraZeneca, in May 2015, we issued 4 ordinary shares to AstraZeneca for aggregate consideration of $100.00.

Amended and Restated Business Transfer and Subscription Agreement and Issuance of A Preference Shares

In May 2015, we and our U.S. subsidiary, Entasis Therapeutics Inc., entered into a Business Transfer and Subscription Agreement with AstraZeneca and certain of its affiliated entities, AstraZeneca UK limited and AstraZeneca Pharmaceuticals LP. AstraZeneca was and is a holder of more than 5% of our outstanding share capital. We amended and restated this agreement in March 2016 and further amended this agreement in August 2017. Pursuant to the terms of this 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. For additional information, including information about our obligation to make milestone and royalty payments to AstraZeneca and certain of its affiliated entities upon the occurrence of specified events, see the section titled "Business—Commercial Agreements—Business Transfer and Subscription Agreement with AstraZeneca."

Transition Services Agreement

In connection with our entry into the Business Transfer and Subscription Agreement, in May 2015 we entered into a Transition Services Agreement with AstraZeneca. Pursuant to this agreement, AstraZeneca agreed to provide us with specified services, including general and administrative functions, such as human resources, information technology and accounting services and research and development activities, including early clinical development and safety studies, as well as regulatory services. We were required to pay AstraZeneca specified amounts per full-time equivalent employee engaged under the agreement, as well as other specified reimbursable expenses. The agreement expired

pursuant to its terms in November 2015. We incurred a total of $0.6 million in expenses for services provided by AstraZeneca under this agreement prior to its expiration.

Cash Management

In connection with the issuance and sale of our A preference shares to AstraZeneca as described above, AstraZeneca agreed to provide cash management services for the net proceeds we received from the sale of such shares for as long as we remained a majority controlled company. As a result, the funds we received upon the closing of the sale of our A preference shares were held by AstraZeneca, as property of our company. This arrangement ceased upon the closing of the sale of 25,000,000 B preference shares in March 2016.

Lease Agreement

In May 2015, our U.S. subsidiary, Entasis Therapeutics Inc., entered into a lease agreement with AstraZeneca Pharmaceuticals LP, an affiliate of AstraZeneca, for 12,805 square feet of leased office, research and development and laboratory facility space in Waltham, Massachusetts. The lease expires in May 2020, with an option to extend the term of the lease for an additional three years. For the period from our inception to December 31, 2015, the years ended December 31, 2016 and December 31, 2017 and the six months ended June 30, 2018, we paid rent of $0.2 million, $0.4 million, $0.4 million and $0.2 million, respectively, under the lease agreement.

In January 2018, we amended the lease agreement, effective February 2, 2018. The amendment extends the lease term through December 31, 2022, and expands the premises to include an additional 7,257 square feet. Under the lease agreement, we have agreed to pay rent totaling $3.1 million over the remaining term of the lease.

AstraZeneca Restricted Stock Units

In connection with their prior employment by AstraZeneca, Drs. Perros and Tommasi received restricted stock units, or RSUs, representing shares in AstraZeneca, pursuant to the AstraZeneca performance share plan, a part of AstraZeneca's long-term incentive program. The RSUs were granted in 2013 and 2014 and were scheduled to vest 36 months following the date of grant or upon a change in control of AstraZeneca. Following our spin-out from AstraZeneca in May 2015, the RSUs continued to vest, with full vesting occurring on March 28, 2017.

Sale of B Preference Shares

In March 2016, we sold an aggregate of 25,000,000 B preference shares at a price of $1.00 per share for an aggregate purchase price of $25.0 million. All of these shares were sold to parties who are now holders of more than 5% of our voting securities and entities affiliated with members of our board of directors. The table below summarizes these sales.

Purchaser	Number of B Preference Shares Purchased	Aggregate Purchase Price
Clarus Lifesciences III, L.P.[1]	7,500,000	$ 7,500,000
Novo Holdings A/S[2]	7,000,000	7,000,000
Frazier Life Sciences VIII, L.P.[3]	7,000,000	7,000,000
Eventide Gilead Fund	3,062,500	3,062,500
Eventide Healthcare & Life Science Fund	437,500	437,500
Total	25,000,000	$25,000,000

(1) Nicholas Galakatos, a member of our board of directors, is a managing director of Clarus.

(2) Thomas Dyrberg, a member of our board of directors, is a managing partner of Novo.

(3) James Topper, a member of our board of directors, is a partner of Frazier Healthcare Partners.

Sale of B-1 Preference Shares

We sold an aggregate of 96,440,678 B-1 preference shares at a price of $0.59 per share in two closings that occurred in August 2017 and December 2017 for an aggregate purchase price of $56.9 million. All of these shares were sold to parties who were or became holders of more than 5% of our voting securities and entities affiliated with members of our board of directors. The table below summarizes these sales.

Purchaser	Number of B-1 Preference Shares Purchased	Aggregate Purchase Price
Clarus Lifesciences III, L.P.(1)	15,254,237	$ 9,000,000
Novo Holdings A/S(2)	14,237,288	8,400,000
Frazier Life Sciences VIII, L.P.(3)	11,864,407	7,000,000
Eventide Gilead Fund	5,190,678	3,062,500
Eventide Healthcare & Life Science Fund	741,525	437,500
Pivotal bioVenture Partners Fund I, L.P.(4)	16,949,153	10,000,000
Sofinnova Venture Partners IX, L.P.(5)	16,949,153	10,000,000
TPG Biotechnology Partners V, L.P.(6)	15,254,237	9,000,000
Total	96,440,678	$56,900,000

(1) Nicholas Galakatos, a member of our board of directors, is a managing director of Clarus.

(2) Thomas Dyrberg, a member of our board of directors, is a managing partner of Novo.

(3) James Topper, a member of our board of directors, is a partner of Frazier Healthcare Partners.

(4) Tracy Saxton, a former member of our board of directors, was the founder and managing partner of Pivotal bioVenture Partners at the time of this sale. Effective December 2017, Robert Hopfner became a member of our board of directors, and is a managing partner of Pivotal bioVenture Partners. Heather Preston, a member of our board of directors, became a managing partner of Pivotal bioVenture Partners in July 2018.

(5) Heather Behanna, a member of our board of directors, is a principal at Sofinnova Ventures.

(6) Heather Preston, a member of our board of directors, is a senior advisor at TPG.

Shareholders' Agreement

In connection with our B-1 preference share financing in August 2017, we entered into an amended and restated shareholders' agreement, as amended, with the holders of our preference shares. The shareholders' agreement, among other things:

- provides for the voting of shares with respect to the constituency of our board of directors and the voting of shares in favor of specified matters approved by our board of directors and the holders of specified percentages of our preference shares;
- obligates us to deliver financial statements and other specified information to some of the holders of our preference shares;
- sets forth specified matters requiring the consent of the holders of our preference shares;
- grants the holders of our preference shares a right of first refusal with respect to sales of our shares by us, subject to specified exclusions, which exclusions include the sale of shares in this offering; and

- grants the holders of our preference shares with specified registration rights, rights of first refusal and tag-along rights with respect to proposed transfers of our securities by other shareholders.

For a description of the registration rights, see the section titled "Shares Eligible for Future Sale—Registration Rights." The shareholders' agreement will automatically terminate upon the completion of this offering.

Management Rights Letters

In March 2016 and August 2017, in connection with our B and B-1 preference share financings, we entered into management rights letters with the purchasers of our preference shares set forth in the tables above. Pursuant to these management rights letters, each entity is entitled to, among other things, consult and advise our management on significant business issues and have access to our books and records and our facilities. Each of these management rights letters will terminate upon the completion of this offering.

Indemnification Agreements

In connection with this offering, we have entered or will enter into indemnification agreements with each of our directors and executive officers. These agreements and our amended and restated certificate of incorporation will require us to indemnify our directors and executive officers to the fullest extent permitted by law. For more information regarding these agreements, see the section titled "Management—Limitation on Liability and Indemnification Matters."

Corporate Reorganization

We completed a corporate reorganization on April 23, 2018. 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. See the section titled "Corporate Reorganization" for more information.

Related Person Transaction Policy

Prior to this offering, we have not had a formal policy regarding approval of transactions with related parties. Prior to the completion of this offering, we expect to adopt a written related person transaction policy that sets forth our procedures for the identification, review, consideration and approval or ratification of related person transactions. The policy will become effective immediately upon the execution of the underwriting agreement for this offering. For purposes of this policy, a related person transaction is a transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we and any related person are, were or will be participants in which the amount involved exceeds $120,000. Transactions involving compensation for services provided to us as an employee or director are not covered by this policy. A related person is any executive officer, director or beneficial owner of more than 5% of any class of our voting securities, including any of their immediate family members and any entity owned or controlled by such persons.

Under the policy, if a transaction has been identified as a related person transaction, including any transaction that was not a related person transaction when originally consummated or any transaction that was not initially identified as a related person transaction prior to consummation, our management must present information regarding the related person transaction to our audit committee, or, if audit committee approval would be inappropriate, to another independent body of our board of directors, for review, consideration and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests, direct and indirect, of the related persons, the benefits to us of the transaction and whether the transaction is on terms that are comparable to the

terms available to or from, as the case may be, an unrelated third party or to or from employees generally. Under the policy, we will collect information that we deem reasonably necessary from each director, executive officer and, to the extent feasible, significant stockholder to enable us to identify any existing or potential related-person transactions and to effectuate the terms of the policy. In addition, under our code of business conduct that we expect to adopt prior to the completion of this offering, our employees and directors will have an affirmative responsibility to disclose any transaction or relationship that reasonably could be expected to give rise to a conflict of interest. In considering related person transactions, our audit committee, or another independent body of our board of directors, will take into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs and benefits to us;
- the impact on a director's independence in the event that the related person is a director, immediate family member of a director or an entity with which a director is affiliated;
- the availability of other sources for comparable services or products; and
- the terms available to or from, as the case may be, unrelated third parties or to or from employees generally.

The policy requires that, in determining whether to approve, ratify or reject a related person transaction, our audit committee, or other independent body of our board of directors, must consider, in light of known circumstances, whether the transaction is in, or is not inconsistent with, our best interests and those of our shareholders, as our audit committee, or other independent body of our board of directors, determines in the good faith exercise of its discretion.

PRINCIPAL STOCKHOLDERS

The following table sets forth the beneficial ownership of our shares as of August 31, 2018 for:

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock;
- each of our named executive officers;
- each of our directors; and
- all of our current executive officers and directors as a group.

The percentage ownership information shown in the table is based upon 8,005,261 shares of our common stock outstanding as of August 31, 2018, after giving effect to the automatic conversion of all outstanding shares of preferred stock, including accrued dividends as of August 31, 2018, into an aggregate of 7,992,622 shares of our common stock upon the completion of this offering. The percentage ownership information under the column titled "After Offering" is based on the sale of 4,411,765 shares of our common stock in this offering. The percentage ownership information assumes no exercise of the underwriters' option to purchase additional shares.

We have determined beneficial ownership in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, the rules include shares issuable pursuant to the exercise of stock options that are exercisable on or before October 30, 2018, which is 60 days after August 31, 2018. These shares are deemed to be outstanding and beneficially owned by the person holding those options for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them, subject to applicable community property laws.

Certain of our stockholders (or their affiliates), including those affiliated with certain of our directors, have indicated an interest in purchasing up to an aggregate of approximately $50.0 million of shares of our common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer, or no shares in this offering to these entities, or these entities may determine to purchase more, fewer, or no shares of common stock in this offering. The following table does not reflect any potential purchases by these potential purchasers. If any shares are purchased by our existing principal stockholders or their affiliated entities, the number and percentage of shares of our common stock beneficially owned by them after this offering will be higher than from those set forth in the following table.

Except as otherwise noted below, the address for persons listed in the table is c/o Entasis Therapeutics Holdings Inc., 35 Gatehouse Drive, Waltham, MA 02451.

Name of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned	
		Before Offering	After Offering
Principal Stockholders:			
AstraZeneca AB[1]	1,876,830	23.4%	15.1%
Clarus Lifesciences III, L.P.[2]	1,158,638	14.5	9.3
Novo Holdings A/S[3]	1,081,393	13.5	8.7
Frazier Life Sciences VIII, L.P.[4]	964,102	12.0	7.8
Pivotal bioVenture Partners Fund I, L.P.[5]	837,800	10.5	6.7
Sofinnova Venture Partners IX, L.P.[6]	837,800	10.5	6.7
TPG Biotechnology Partners V, L.P.[7]	754,021	9.4	6.1
Entities affiliated with Eventide Gilead Fund[8]	482,046	6.0	3.9
Named Executive Officers and Directors:			
Manoussos Perros, Ph.D.[9]	173,275	2.1	1.4
Michael Gutch, Ph.D.[10]	22,720	*	*
Robin Isaacs, M.D.[11]	38,007	*	*
Nicholas Galakatos, Ph.D.[12]	1,158,638	14.5	9.3
Heather Behanna, Ph.D.[13]	—	—	—
Thomas Dyrberg, M.D., D.M.Sc.[14]	—	—	—
David C. Hastings[15]	—	—	—
Robert Hopfner, Ph.D.[16]	837,800	10.5	6.7
Gregory Norden[17]	6,115	*	*
Heather Preston, M.D.[18]	837,800	10.5	6.7
Andrew J. Staples[19]	—	—	—
James N. Topper, M.D., Ph.D.[20]	964,102	12.0	7.8
All current directors and executive officers as a group (14 persons)[21]	4,118,566	49.5	32.3

* Represents beneficial ownership of less than 1%.

(1) Consists of 4 shares of common stock and 1,876,822 shares of common stock issuable upon conversion of the Series A preferred stock. The principal business address of AstraZeneca AB is SE-151, 85 Sodertalje, Sweden.

(2) Consists of 404,617 shares of common stock issuable upon conversion of the Series B preferred stock and 754,021 shares issuable upon conversion of the Series B-1 preferred stock. Clarus Ventures III GP, L.P., or Clarus III GP, is the sole general partner of Clarus Lifesciences III, L.P., or Clarus III. Clarus Ventures III, LLC, or Clarus III GPLLC, is the sole general partner of Clarus III GP. Nicholas Galakatos, Dennis Henner, Robert Liptak, Nicholas Simon, Scott Requadt and Kurt Wheeler, or the Managers, are all of the managing directors of Clarus III GPLLC. As the general partner of Clarus III, Clarus III GP may be deemed to own beneficially the shares held by Clarus III. As the general partner of Clarus III GP, Clarus III GPLLC likewise may be deemed to own beneficially the shares held by Clarus III. As the managing directors of Clarus III GPLLC, each of the Managers also may be deemed to own beneficially the shares held by Clarus III. Each of Messrs. Galakatos, Henner, Liptak, Simon, Requadt and Wheeler disclaims beneficial ownership of all shares held of record by Clarus in which he does not have an actual pecuniary interest. The principal business address of Clarus Lifesciences III, L.P. is 101 Main Street, Suite 1210, Cambridge, MA 02142.

(3) Consists of 377,642 shares of common stock issuable upon conversion of the Series B preferred stock and 703,751 shares of common stock issuable upon conversion of the Series B-1 preferred stock. The board of directors of Novo Holdings A/S, or Novo, consists of Viviane Monges, Jeppe Christiansen, Steen Riisgaard, Lars Rebien Sørensen, Jean-Luc Butel and Francis Cuss, who share investment and voting control with respect to the shares held by Novo and may exercise such control only with the support of a majority of the members of the Novo board of directors. No individual member of the Novo board of directors is deemed to

hold any beneficial ownership or reportable pecuniary interest in the shares held by Novo. The principal business address of Novo is Tuborg Havnevej 19, DK-2900 Hellerup, Denmark.

(4) Consists of 377,642 shares of common stock issuable upon conversion of the Series B preferred stock and 586,460 shares of common stock issuable upon conversion of the Series B-1 preferred stock. The general partner of Frazier Life Sciences VIII, LP, or FLS LP, is FHM Life Sciences VIII, LP, or FHM LP. The general partner of FHM LP is FHM Life Sciences VIII, LLC, or FHM LLC. James Topper and Patrick Heron are the sole managing members of FHM LLC and share voting and investment power with respect to the shares held by FLS LP. Dr. Topper and Mr. Heron disclaim beneficial ownership of such shares except to the extent of their pecuniary interest in such shares. The principal business address of FLS LP is Two Union Square, 601 Union Street, Suite 3200, Seattle, WA 98101.

(5) Consists of 837,800 shares of common stock issuable upon conversion of the Series B-1 preferred stock. The general partner of Pivotal bioVenture Partners Fund I, L.P., or Pivotal, is Pivotal bioVenture Partners Fund I G.P., L.P., or Pivotal GP. The general partner of Pivotal GP is Pivotal bioVenture Partners Fund I U.G.P., Ltd, or the Ultimate General Partner. Richard Coles, Peter Bisgaard and Vincent Sai Sing Cheung are directors of the Ultimate General Partner and may, along with the Ultimate General Partner, be deemed to have shared voting and dispositive power over the shares owned by Pivotal. The principal business address of Pivotal is 1700 Owens Street, Suite 595, San Francisco, CA 94158.

(6) Consists of 837,800 shares of common stock issuable upon conversion of the Series B-1 preferred stock. Sofinnova Management IX, L.L.C. is the general partner of Sofinnova Venture Partners IX, L.P., or SVP IX, and James I. Healy, Michael F. Powell and Anand Mehra, the managing members thereof, share investment and disposition powers of the shares held by SVP IX. Such persons disclaim beneficial ownership of such shares except to the extent of their pecuniary interest therein. The principal business address of SVP IX is 3000 Sand Hill Road, Building 4, Suite 250, Menlo Park, CA 94025.

(7) Consists of 754,021 shares of common stock issuable upon conversion of the Series B-1 preferred stock. The general partner of TPG Biotechnology Partners V, L.P., or TPG Biotech V, is TPG Biotechnology GenPar V, L.P., whose general partner is TPG Biotechnology GenPar V Advisors, LLC, whose sole member is TPG Holdings I, L.P., whose general partner is TPG Holdings I-A, LLC, whose sole member is TPG Group Holdings (SBS), L.P., whose general partner is TPG Group Holdings (SBS) Advisors, LLC, whose sole member is TPG Group Holdings (SBS) Advisors, Inc. David Bonderman and James G. Coulter are sole shareholders of TPG Group Holdings (SBS) Advisors, Inc. and may therefore be deemed to be the beneficial owners of the shares held by TPG Biotech V. Messrs. Bonderman and Coulter disclaim beneficial ownership of the shares held by TPG Biotech V except to the extent of their pecuniary interest therein. The principal business address of TPG Biotech V is 301 Commerce Street, Suite 3300, Fort Worth, TX 76102.

(8) Consists of (i) 165,218 shares of common stock issuable upon conversion of Series B preferred stock and 256,575 shares of common stock issuable upon conversion of the Series B-1 preferred stock held by Eventide Gilead Fund and (ii) 23,601 shares of common stock issuable upon conversion of Series B preferred stock and 36,652 shares of common stock issuable upon conversion of Series B-1 preferred stock held by Eventide Healthcare & Life Science Fund. Eventide Gilead Fund and Eventide Healthcare & Life Sciences Fund are registered investment companies for which Eventide Asset Management, LLC acts as investment advisor. Eventide Asset Management, LLC has voting and investment power with respect to the shares. The principal business address of each of Eventide Gilead Fund and Eventide Healthcare & Life Science Fund is One International Place, Suite #3510, Boston, MA 02110.

(9) Consists of 173,275 shares of common stock issuable upon the exercise of outstanding options exercisable within 60 days of August 31, 2018.

(10) Consist of 22,720 shares of common stock issuable upon the exercise of outstanding options exercisable within 60 days of August 31, 2018.

(11) Consists of 38,007 shares of common stock issuable upon the exercise of outstanding options exercisable within 60 days of August 31, 2018.

(12) Consists of 404,617 shares of common stock issuable upon conversion of Series B preferred stock and 754,021 shares of common stock issuable upon conversion of Series B-1 preferred stock. Clarus Ventures III GP, L.P., or Clarus III GP, is the sole general partner of Clarus III. Clarus III GPLLC is the sole general partner of Clarus III GP. Nicholas Galakatos, Dennis Henner, Robert Liptak, Nicholas Simon, Scott Requadt and Kurt Wheeler, or the Managers, are all of the managing directors of Clarus III GPLLC. As the general partner of Clarus III, Clarus III GP may be deemed to own beneficially the shares held by Clarus III. As the general partner of Clarus III GP, Clarus III GPLLC likewise may be deemed to own beneficially the shares held by Clarus III. As the managing directors of Clarus III GPLLC, each of the Managers also may be deemed to

own beneficially the shares held by Clarus III. Each of Messrs. Galakatos, Henner, Liptak, Simon, Requadt and Wheeler disclaims beneficial ownership of all shares held of record by Clarus in which he does not have an actual pecuniary interest. The principal business address of Clarus Lifesciences III, L.P. is 101 Main Street, Suite 1210, Cambridge, MA 02142.

(13) Dr. Behanna is a principal at Sofinnova Ventures. Dr. Behanna is not deemed to have any beneficial ownership in the shares held by SVP IX listed in footnote 6 above.

(14) Dr. Dyrberg is a managing partner of Novo. Dr. Dyrberg is not deemed to have any beneficial ownership or reportable pecuniary interest in the shares held by Novo listed in footnote 3 above.

(15) Mr. Hastings is not deemed to have beneficial ownership over any shares.

(16) Consists of 837,800 shares of common stock issuable upon conversion of Series B-1 preferred stock held by Pivotal. Dr. Hopfner is a managing partner of Pivotal bioVenture Partners Management Ltd., or the Investment Advisor, which is the investment advisor to Pivotal, and is managing partner of Pivotal bioVenture Partners Investment Advisor, LLC, which is the U.S. sub-advisor to the Investment Advisor. Therefore, Dr. Hopfner may be deemed to beneficially own the shares held by Pivotal. The principal business address of Pivotal bioVenture Partners Fund I, L.P. is 1700 Owens Street, Suite 595, San Francisco, CA 94158.

(17) Consists of 6,115 shares of common stock issuable upon the exercise of outstanding options exercisable within 60 days of August 31, 2018.

(18) Consists of 837,800 shares of common stock issuable upon conversion of Series B-1 preferred stock held by Pivotal. Dr. Preston is a managing partner of Investment Advisor, which is the investment advisor to Pivotal, and is managing partner of Pivotal bioVenture Partners Investment Advisor, LLC, which is the U.S. sub-advisor to the Investment Advisor. Therefore, Dr. Preston may be deemed to beneficially own the shares held by Pivotal. The principal address of Pivotal bioVenture Partners Fund I, L.P. is 1700 Owens Street, Suite 595, San Francisco, CA 94158. Dr. Preston is a also senior advisor at TPG Biotech V. Dr. Preston is not deemed to have any beneficial ownership or reportable pecuniary interest in the shares held by TPG Biotech V listed in footnote 7 above.

(19) Mr. Staples is head of deal finance of AstraZeneca AB. Mr. Staples is not deemed to have any beneficial ownership or reportable pecuniary interest in the shares held by AstraZeneca AB listed in footnote 1 above.

(20) Consists of 377,642 shares of common stock issuable upon conversion of Series B preferred stock and 586,460 shares of common stock issuable upon conversion of Series B-1 preferred stock. The general partner of FLS LP is FHM LP. The general partner of FHM LP is FHM LLC. James Topper and Patrick Heron are the sole managing members of FHM LLC and share voting and investment power with respect to the shares held by FLS LP. Dr. Topper and Mr. Heron disclaim beneficial ownership of such shares except to the extent of their pecuniary interest in such shares. The principal business address of FLS LP is Two Union Square, 601 Union Street, Suite 3200, Seattle, WA 98101.

(21) Consists of (i) 782,259 shares of common stock issuable upon conversion of Series B preferred stock, (ii) 2,178,281 shares of common stock issuable upon conversion of Series B-1 preferred stock and (iii) 320,226 shares of common stock issuable upon the exercise of outstanding options exercisable within 60 days of August 31, 2018.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries. You should also refer to the amended and restated certificate of incorporation, the amended and restated bylaws and the registration rights agreement, which are filed as exhibits to the registration statement of which this prospectus is part.

General

Upon the completion of this offering and filing of our amended and restated certificate of incorporation, our authorized capital will consist of 125,000,000 shares of common stock, par value $0.001 per share, and 10,000,000 shares of preferred stock, par value $0.001 per share.

Common Stock

Outstanding Shares

As of June 30, 2018, we had 8,005,261 shares of common stock outstanding, held of record by 14 stockholders, after giving effect to the automatic conversion of all outstanding shares of our preferred stock, including accrued dividends as of August 31, 2018, into shares of common stock upon the completion of this offering.

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders. The affirmative vote of holders of at least 66⅔% of the voting power of all of the then-outstanding shares of capital stock, voting as a single class, will be required to amend certain provisions of our amended and restated certificate of incorporation, including provisions relating to amending our amended and restated bylaws, the classified board, the size of our board, removal of directors, director liability, vacancies on our board, special meetings, stockholder notices, actions by written consent and exclusive forum.

Dividends

Subject to preferences that may apply to any outstanding preferred stock, holders of our common stock are entitled to receive ratably any dividends that our board of directors may declare out of funds legally available for that purpose.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any outstanding preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully Paid and Nonassessable

All outstanding shares of our common stock are fully paid and non-assessable, and the shares of common stock to be issued upon completion of this offering will be fully paid and non-assessable.

Preferred Stock

Immediately prior to the completion of this offering, all outstanding shares of our preferred stock will convert into shares of common stock. Upon completion of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the number, rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences and sinking fund terms, and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control or other corporate action. We have no current plan to issue any shares of preferred stock.

Stock Options

As of June 30, 2018, 1,168,938 shares of common stock were issuable upon the exercise of outstanding stock options, at a weighted-average exercise price of $4.70 per share. For additional information regarding terms of our equity incentive plans, see the section titled "Executive and Director Compensation—Equity Incentive Plans."

Registration Rights

Upon the completion of this offering, holders of shares of our common stock issuable upon the conversion of our preferred stock, including any accrued dividends thereon, in connection with this offering will initially be entitled to certain rights with respect to registration of such shares under the Securities Act. These shares are referred to as registrable securities. The holders of these registrable securities possess registration rights pursuant to the terms of our registration rights agreement and are described in additional detail below. The registration of shares of our common stock pursuant to the exercise of the registration rights described below would enable the holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective. We will pay the registration expenses, other than underwriting discounts, selling commissions and stock transfer taxes, of up to $50,000 for the shares registered pursuant to the demand, piggyback and Form S-3 registrations described below.

Generally, in an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to limit the number of shares the holders may include. The demand, piggyback and Form S-3 registration rights described below will expire no later than five years after the completion of this offering, or with respect to any particular holder, at such time that such holder can sell all of its shares under Rule 144 of the Securities Act during any three-month period.

Demand Registration Rights

Upon the completion of this offering, holders of 7,992,622 shares of our common stock issuable upon conversion of all of our outstanding preferred stock, including the accrued dividends as of August 31, 2018, plus any shares of common stock paid pursuant to any dividends accruing from September 1, 2018 through the day immediately prior to the closing of this offering, will be entitled to certain demand registration rights. At any time beginning 180 days following the effectiveness of this

registration statement, the holders of at least 30% of registrable securities then outstanding (or a lesser percent if the anticipated aggregate offering price, net of selling expenses, would exceed $15,000,000) may, on not more than one occasion, request that we register all or a portion of their shares, subject to certain specified exceptions.

Piggyback Registration Rights

Following this offering, holders of 7,992,622 shares of our common stock issuable upon conversion of all of our outstanding preferred stock, including the accrued dividends as of August 31, 2018, plus any shares of common stock paid pursuant to any dividends accruing from September 1, 2018 through the day immediately prior to the closing of this offering, will be entitled to include their shares of registrable securities in any registration statement we file in the event that we propose to register any of our securities under the Securities Act in an offering, either for our own account or for the account of other security holders, subject to specified conditions and limitations.

S-3 Registration Rights

Upon the completion of this offering, the holders of 7,992,622 shares of our common stock issuable upon conversion of all of our outstanding preferred stock, including the accrued dividends as of August 31, 2018, plus any shares of common stock paid pursuant to any dividends accruing from September 1, 2018 through the day immediately prior to the closing of this offering, will initially be entitled to certain Form S-3 registration rights. One or more holders may, on not more than two occasions within any 12-month period, request that we register all or a portion of their shares on Form S-3 if we are qualified to file a registration statement on Form S-3, subject to specified exceptions. Such request for registration on Form S-3 must cover securities with an aggregate offering price which equals or exceeds $3.0 million, net of selling expenses. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Indemnification

The registration rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

Anti-Takeover Provisions

Certificate of Incorporation and Bylaws to be in Effect Immediately Prior to Completion of this Offering

Our amended and restated certificate of incorporation and amended and restated bylaws, each to become effective immediately prior to the completion of this offering, will:

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate, including the right to approve an acquisition or other change in control;
- provide that the authorized number of directors may be changed only by resolution of our board of directors;
- provide that our board of directors will be classified into three classes of directors;
- provide that, subject to the rights of any series of preferred stock to elect directors, directors may only be removed for cause, which removal may be effected, subject to any limitation imposed by law, by the holders of at least 66⅔% of the voting power of all of our then-outstanding shares of the capital stock entitled to vote generally at an election of directors;

- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent or electronic transmission;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder's notice;
- provide that special meetings of our stockholders may be called only by the chairman of our board of directors, our chief executive officer or president or by our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors; and
- not provide for cumulative voting rights, therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose.

The amendment of any of these provisions would require approval by the holders of at least 66⅔% of the voting power of all of our then-outstanding common stock entitled to vote generally in the election of directors, voting together as a single class.

The combination of these provisions will make it more difficult for our existing stockholders to replace our board of directors as well as for another party to obtain control of us by replacing our board of directors. Because our board of directors has the power to retain and discharge our officers, these provisions could also make it more difficult for existing stockholders or another party to effect a change in management. In addition, the authorization of undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change our control.

These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and its policies and to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to reduce our vulnerability to hostile takeovers and to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and may have the effect of delaying changes in our control or management. As a consequence, these provisions may also inhibit fluctuations in the market price of our stock that could result from actual or rumored takeover attempts. We believe that the benefits of these provisions, including increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure our company, outweigh the disadvantages of discouraging takeover proposals, because negotiation of takeover proposals could result in an improvement of their terms.

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the DGCL, which prohibits a Delaware corporation from engaging in a business combination with any interested stockholder for a period of three years following the date the person became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested holder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the

corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (a) by persons who are directors and also officers and (b) pursuant to employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; and

- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 66⅔% of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 of the DGCL defines business combination to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 of the DGCL defines an "interested stockholder" as an entity or person who, together with the entity's or person's affiliates and associates, beneficially owns, or is an affiliate of the corporation and within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

The statute could prohibit or delay mergers or other takeover or change in control attempts and, accordingly, may discourage attempts to acquire us even though such a transaction may offer our stockholders the opportunity to sell their stock at a price above the prevailing market price.

A Delaware corporation may "opt out" of these provisions with an express provision in its certificate of incorporation. We have not opted out of these provisions, which may as a result, discourage or prevent mergers or other takeover or change of control attempts of us.

Choice of Forum

Our amended and restated certificate of incorporation will provide that the Court of Chancery of the State of Delaware will be 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 that is governed by the internal affairs doctrine. Our amended and restated certificate of incorporation will further provide 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. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings

described above, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable.

Transfer Agent and Registrar

Our transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Nasdaq Global Market Listing

We have applied to list our common stock on The Nasdaq Global Market under the trading symbol "ETTX."

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, no public market existed for our common stock. Future sales of our common stock in the public market after this offering, or the perception that these sales could occur, could adversely affect prevailing market prices for our common stock and could impair our future ability to raise equity capital.

Based on the number of shares outstanding as of June 30, 2018, upon completion of this offering and assuming no exercise of the underwriters' option to purchase additional shares, 12,417,026 shares of our common stock will be outstanding, after giving effect to the issuance of 4,411,765 shares offered by us in this offering and the automatic conversion of all outstanding preferred stock, including accrued dividends as of August 31, 2018, into 7,992,622 shares of our common stock upon the completion of this offering. All of the shares of our common stock sold in this offering will be freely tradable without restrictions or further registration under the Securities Act of 1933, as amended, or the Securities Act, except for any shares sold to our "affiliates," as that term is defined under Rule 144 under the Securities Act. The remaining shares of our common stock held by existing stockholders are "restricted securities," as that term is defined in Rule 144 under the Securities Act. Restricted securities may be sold in the public market only if registered or if their resale qualifies for exemption from registration described below under Rule 144 promulgated under the Securities Act.

As a result of contractual restrictions described below and the provisions of Rules 144 and 701, the shares sold in this offering and the restricted securities will be available for sale in the public market as follows:

- the 4,411,765 shares sold in this offering will be eligible for immediate sale upon the completion of this offering, except shares purchased by our affiliates, which would be subject to the limitations described below; and
- approximately 8,005,261 restricted shares will be eligible for sale in the public market upon expiration of lock-up agreements 180 days after the date of this prospectus, subject in certain circumstances to the volume, manner of sale and other limitations under Rule 144 and Rule 701.

Rule 144

In general, persons who have beneficially owned restricted shares of our common stock for at least six months, and any affiliate of the company who owns either restricted or unrestricted shares of our common stock, are entitled to sell their securities without registration with the SEC under an exemption from registration provided by Rule 144 under the Securities Act.

Non-Affiliates

Any person who is not deemed to have been one of our affiliates at the time of, or at any time during the three months preceding, a sale may sell an unlimited number of restricted securities under Rule 144 if:

- the restricted securities have been held for at least six months, including the holding period of any prior owner other than one of our affiliates;
- we have been subject to the Securities Exchange Act of 1934, as amended, or the Exchange Act, periodic reporting requirements for at least 90 days before the sale; and
- we are current in our Exchange Act reporting at the time of sale.

Any person who is not deemed to have been an affiliate of ours at the time of, or at any time during the three months preceding, a sale and has held the restricted securities for at least one year, including the holding period of any prior owner other than one of our affiliates, will be entitled to sell

an unlimited number of restricted securities without regard to the length of time we have been subject to Exchange Act periodic reporting or whether we are current in our Exchange Act reporting.

Affiliates

Persons seeking to sell restricted securities who are our affiliates at the time of, or any time during the three months preceding, a sale, would be subject to the restrictions described above. They are also subject to additional restrictions, by which such person would be required to comply with the manner of sale and notice provisions of Rule 144 and would be entitled to sell within any three-month period only that number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 125,000 shares immediately after the completion of this offering based on the number of shares outstanding as of June 30, 2018; or
- the average weekly trading volume of our common stock on The Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Additionally, persons who are our affiliates at the time of, or any time during the three months preceding, a sale may sell unrestricted securities under the requirements of Rule 144 described above, without regard to the six month holding period of Rule 144, which does not apply to sales of unrestricted securities.

Rule 701

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares. However, substantially all Rule 701 shares are subject to lock-up agreements as described below and in the section of this prospectus titled "Underwriting" and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

Form S-8 Registration Statements

As of June 30, 2018, we had outstanding options to purchase 1,168,938 shares of our common stock (which excludes stock options to be granted upon the pricing of this offering). As soon as practicable after the completion of this offering, we intend to file with the SEC one or more registration statements on Form S-8 under the Securities Act to register the shares of our common stock that are issuable pursuant to our 2015 Plan, 2018 Plan and ESPP. These registration statements will become effective immediately upon filing. Shares covered by these registration statements will then be eligible for sale in the public markets, subject to vesting restrictions, any applicable lock-up agreements described below and Rule 144 limitations applicable to affiliates.

Lock-Up Agreements

We and the holders of substantially all of the shares of our common stock outstanding on the date of this prospectus, including each of our executive officers and directors, have entered into lock-up agreements with the underwriters or otherwise agreed, subject to certain exceptions, that we and they will not, directly or indirectly, offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale, or otherwise dispose of or hedge any of our shares of our common stock, any options or warrants to purchase shares of our common stock, or any securities convertible into, or exchangeable

for or that represent the right to receive shares of our common stock, without the prior written consent of the representatives of the underwriters for a period of 180 days from the date of this prospectus.

Registration Rights

Upon the completion of this offering, the holders of 7,992,622 shares of our common stock will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described under "—Lock-Up Agreements" above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock. See the section titled "Description of Capital Stock—Registration Rights."

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following discussion is a summary of material U.S. federal income tax considerations relating to ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term "non-U.S. holder" means a beneficial owner (other than a partnership or other pass-through entity) of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or of any state thereof or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through (or disregarded) entities for U.S. federal income tax purposes or persons who hold their common stock through partnerships or such other pass-through or disregarded entities. The tax treatment of a partner in an entity or arrangement that is treated as a partnership for U.S. federal income tax purposes generally will depend upon the status of the partner and the activities of the partnership. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the Internal Revenue Code of 1986, as amended, or the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, and current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus, and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described in this prospectus.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a capital asset (generally, property held for investment) for U.S. federal income tax purposes. This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes, the alternative minimum tax, the estate or gift taxes or the Medicare tax on net investment income. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- financial institutions;
- brokers or dealers in securities;
- tax-exempt organizations;
- pension plans;

- owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
- traders in securities that have elected the mark-to-market method of accounting for their securities holdings;
- insurance companies;
- controlled foreign corporations;
- passive foreign investment companies;
- persons that have a functional currency other than the U.S. dollar;
- persons who have acquired our common stock pursuant to the exercise of an option or otherwise in a compensatory transaction;
- non-U.S. governments; and
- certain U.S. expatriates.

THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT, AND IS NOT INTENDED TO BE, LEGAL OR TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE U.S. FEDERAL, STATE, LOCAL AND NON-U.S. INCOME, ESTATE AND OTHER TAX CONSIDERATIONS OF ACQUIRING, HOLDING AND DISPOSING OF OUR COMMON STOCK. IN ADDITION, SIGNIFICANT CHANGES IN U.S. FEDERAL INCOME TAX LAWS WERE RECENTLY ENACTED. YOU SHOULD ALSO CONSULT WITH YOUR TAX ADVISOR WITH RESPECT TO SUCH CHANGES IN U.S. TAX LAW AS WELL AS POTENTIAL CONFORMING CHANGES IN STATE TAX LAWS.

Distributions on Our Common Stock

As discussed under "*Dividend Policy*" above, we do not expect to make cash dividends to holders of our common stock in the foreseeable future. Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to the holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading "*Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock*." Any such distributions will also be subject to the discussion below under the headings "*Information Reporting and Backup Withholding*" and "*FATCA*."

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements (generally including provision of a valid IRS Form W-8ECI (or applicable successor form) certifying that the dividends are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States). However, such U.S. effectively connected income, net of specified deductions and credits, is taxed in the hands of the non-U.S. holder at the same corporate or graduated individual U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a

non-U.S. holder that is classified as a corporation for U.S. federal income tax purposes may also be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty and the specific methods available to them to satisfy these requirements.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock

Subject to the discussion below under the headings "*Information Reporting and Backup Withholding*" and "*FATCA*," a non-U.S. holder generally will not be subject to U.S. federal income tax or withholding tax on any gain realized upon such non-U.S. holder's sale, exchange or other taxable disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the corporate or graduated individual U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "*Distributions on Our Common Stock*" also may apply;
- the non-U.S. holder is a non-resident alien individual present in the United States for a period or periods aggregating 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S.-source capital losses of the non- U.S. holder recognized in the taxable year of the disposition, if any; or
- we are, or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation" unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, at any time during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a "U.S. real property holding corporation" if the fair market value of its "U.S. real property interests" (as defined in the Code and applicable Treasury Regulations) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we believe that we are not currently, and we do not anticipate becoming, a "U.S. real property holding corporation" for U.S. federal income tax purposes. If we are a U.S. real property holding corporation and either our common stock is not regularly traded on an established securities market or a non-U.S. holder holds more than 5% of our outstanding common stock, directly or indirectly, during the applicable testing period, such non-U.S. holder's gain on the disposition of shares of our common stock generally will be taxed in the same manner as gain that is effectively connected

with the conduct of a U.S. trade or business, except that the branch profits tax generally will not apply. If we are a U.S. real property holding corporation and our common stock is not regularly traded on an established securities market, a non-U.S. holder's proceeds received on the disposition of shares will also generally be subject to withholding at a rate of 15%. Prospective investors are encouraged to consult their own tax advisors regarding the possible consequences to them if we are, or were to become, a U.S. real property holding corporation.

Information Reporting and Backup Withholding

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders generally will have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Generally, a non-U.S. holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable Form W-8), or otherwise meets the documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption (and the payor does not have actual knowledge or reason to know that such holder is a United States person). Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above under "*Distributions on Our Common Stock*," will generally be exempt from U.S. backup withholding.

Information reporting and backup withholding, currently at a rate of 24%, generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, whether U.S. or non-U.S., unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption from backup withholding. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

FATCA

The Foreign Account Tax Compliance Act, or FATCA, generally imposes a 30% withholding tax on dividends on, and gross proceeds from the sale or disposition of, our common stock paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," the foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," the foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt from FATCA.

Withholding under FATCA generally applies (1) to payments of dividends on our common stock, and (2) to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2018. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Under certain

circumstances, a non-U.S. holder may be eligible for refunds or credits of the tax. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

The preceding discussion of material U.S. federal tax considerations is for informational purposes only. It is not legal or tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed or recently enacted changes in applicable laws.

UNDERWRITING

Under the terms and subject to the conditions contained in an underwriting agreement dated , 2018, we have agreed to sell to the underwriters named below, for whom Credit Suisse Securities (USA) LLC and BMO Capital Markets Corp. are acting as representatives, the following respective numbers of shares of common stock:

Underwriter	Number of Shares
Credit Suisse Securities (USA) LLC	
BMO Capital Markets Corp.	
SunTrust Robinson Humphrey, Inc.	
Wedbush Securities Inc.	
Total	4,411,765

The underwriting agreement provides that the underwriters are obligated to purchase all the shares of common stock in the offering if any are purchased, other than those shares covered by the option described below. The underwriting agreement also provides that if an underwriter defaults the purchase commitments of non-defaulting underwriters may be increased or the offering may be terminated.

Certain of our stockholders (or their affiliates), including those affiliated with certain of our directors, have indicated an interest in purchasing up to an aggregate of approximately $50.0 million of shares of our common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer, or no shares in this offering to these entities, or these entities may determine to purchase more, fewer, or no shares of common stock in this offering. The underwriters will receive the same underwriting discounts and commissions on any shares of common stock purchased by these entities as they will on any other shares of common stock sold to the public in this offering.

We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

We have granted to the underwriters a 30-day option to purchase on a pro rata basis up to 661,764 additional shares of common stock at the initial public offering price less the underwriting discounts and commissions. The option may be exercised only to cover any over-allotments of common stock.

The underwriters propose to offer the shares of common stock initially at the public offering price on the cover page of this prospectus and to selling group members at that price less a selling concession of up to $ per share. After the initial public offering the underwriters may change the public offering price and selling concession.

The following table summarizes the compensation and estimated expenses we will pay:

	Per Share		Total	
	Without Option	With Option	Without Option	With Option
Underwriting discounts and commissions paid by us	$	$	$	$
Expenses payable by us	$	$	$	$

We have also agreed to reimburse the underwriters in an amount up to $25,000 for legal fees and expenses relating to clearance of this offering with the Financial Industry Regulatory Authority, or

FINRA. In accordance with FINRA Rule 5110, these reimbursed fees and expenses are deemed underwriting compensation for this offering.

We have agreed, subject to certain exceptions, that we will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, or file with the Securities and Exchange Commission a registration statement under the Securities Act relating to, any shares of our our common stock, or securities convertible into or exchangeable or exercisable for shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, without the prior written consent of the representatives for a period of 180 days after the date of this prospectus.

Our officers, directors and holders of substantially all of our common stock and securities exercisable for or convertible into our our common stock outstanding immediately prior to this offering have agreed, subject to certain exceptions, that they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any shares of our common stock, or securities convertible into or exchangeable or exercisable for any shares of our common stock, enter into a transaction that would have the same effect, or enter into any swap, hedge or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock, whether any of these transactions are to be settled by delivery of our common stock or other securities, in cash or otherwise, or publicly disclose the intention to make any offer, sale, pledge or disposition, or to enter into any transaction, swap, hedge or other arrangement, without, in each case, the prior written consent of the representatives for a period of 180 days after the date of this prospectus.

We have applied to list our common stock on The Nasdaq Global Market.

Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiations among us and the representatives and will not necessarily reflect the market price of the common stock shares following this offering. The principal factors that will be considered in determining the initial public offering price include:

- the information presented in this prospectus and otherwise available to the underwriters;
- the history of, and prospects for, the industry in which we will compete;
- the ability of our management;
- the prospects for our future earnings;
- the present state of our development, results of operations and our current financial condition;
- the general condition of the securities markets at the time of this offering; and
- the recent market prices of, and the demand for, publicly traded equity securities of generally comparable companies.

We cannot assure you that the initial public offering price will correspond to the price at which our common stock will trade in the public market subsequent to this offering or that an active trading market for our common stock will develop and continue after this offering.

In connection with the offering the underwriters may engage in stabilizing transactions, over-allotment transactions, syndicate covering transactions and penalty bids in accordance with Regulation M under the Exchange Act.

- Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum.
- Over-allotment involves sales by the underwriters of shares in excess of the number of shares the underwriters are obligated to purchase, which creates a syndicate short position. The short position may be either a covered short position or a naked short position. In a covered short

position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the over-allotment option. In a naked short position, the number of shares involved is greater than the number of shares in the over-allotment option. The underwriters may close out any covered short position by either exercising their over-allotment option and/or purchasing shares in the open market.

- Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option. If the underwriters sell more shares than could be covered by the over-allotment option, a naked short position, the position can only be closed out by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there could be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.
- Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the shares of common stock originally sold by the syndicate member is purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of the common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. These transactions may be effected on The Nasdaq Global Market or otherwise and, if commenced, may be discontinued at any time.

A prospectus in electronic format may be made available on the web sites maintained by one or more of the underwriters, or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations.

Conflicts of Interest

The underwriters and their respective affiliates are full-service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

The underwriters do not expect to sell more than 5% of the shares in the aggregate to accounts over which they exercise discretionary authority.

Selling Restrictions

General

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection

with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Canada

Shares of our common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the Securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the Securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor. Pursuant to section 3A-3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriters conflicts of interest in connection with this offering.

United Kingdom

This document is only being distributed to and is only directed at persons who are "qualified investors" (as defined in the Prospectus Directive) who are (i) persons having professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order, (ii) high net worth entities, and (iii) other persons to whom it may lawfully be communicated, falling with Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). The securities are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire such securities will be engaged in only with, relevant persons. This document and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by any recipients to any other person in the United Kingdom. Any person who is not a relevant person should not act or rely on this document or any of its contents.

European Economic Area

In relation to each Member State of the European Economic Area that has implemented the Prospectus Directive (each, a "Relevant Member State"), an offer to the public of any securities described in this prospectus may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any ordinary shares may be made at any time under the following exemptions under the Prospectus Directive if they have been implemented in that Relevant Member State:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) per Relevant Member State, subject to obtaining the prior consent of the underwriters; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive;

provided that no such offer of securities described in this prospectus shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive or a supplemental prospectus pursuant to Article 16, of the Prospectus Directive or any measure implementing the Prospectus Directive in a Relevant Member State and each person who initially acquires any securities or to whom any offer is made on the basis of (a) above will be deemed to have represented, acknowledged and agreed that it is a "qualified investor" within the meaning of Article 2(1)(e) of this Prospectus Directive.

For the purposes of this provision, the expression an "offer of securities to the public" in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Relevant Member State. The expression "Prospectus Directive" means Directive 2003/71/EC (as amended, including by Directive 2010/73/EU) and includes any relevant implementing measure in each Relevant Member State.

Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or the SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the Company, or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or the CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

China

This prospectus does not constitute a public offer of the shares offered by this prospectus, whether by sale or subscription, in China. The shares are not being offered or sold directly or indirectly in China to or for the benefit of, legal or natural persons of the PRC.

Further, no legal or natural persons of China may directly or indirectly purchase any of the shares without obtaining all prior Chinese governmental approvals that are required, whether statutorily or otherwise. Persons who come into possession of this prospectus are required by the issuer and its representatives to observe these restrictions.

Hong Kong

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap.32, Laws of Hong Kong), or (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap.32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

LEGAL MATTERS

The validity of the shares being offered by this prospectus will be passed upon for us by Cooley LLP, Washington, D.C. Certain legal matters related to this offering will be passed upon for the underwriters by Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York.

EXPERTS

The consolidated financial statements of Entasis Therapeutics Limited as of December 31, 2016 and 2017, and for the years then ended have been included herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, appearing elsewhere herein, and upon the authority of said firm as experts in accounting and auditing.

The audit report covering the December 31, 2017 consolidated financial statements contains an explanatory paragraph that states that the Company's recurring losses and negative cash flows from operations raise substantial doubt about the entity's ability to continue as a going concern. The consolidated financial statements do not include any adjustments that might result from the outcome of that uncertainty.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act, with respect to the shares of common stock being offered by this prospectus. This prospectus, which constitutes part of the registration statement, does not contain all of the information in the registration statement and its exhibits. For further information with respect to our company and the shares offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You may read our SEC filings, including the registration statement, over the internet at the SEC's website at *www.sec.gov*. You may also read and copy any document we file with the SEC at its public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

Upon completion of this offering, we will be subject to the information reporting requirements of the Exchange Act, and we will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above. 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 prospectus.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and Board of Directors
Entasis Therapeutics Limited:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Entasis Therapeutics Limited and subsidiary (the Company) as of December 31, 2016 and 2017, the related consolidated statements of operations, redeemable convertible preference shares and shareholders' 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, 2016 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.

Going Concern

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

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. 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 23, 2018, except as to the reverse stock split described in note 2, which is as of September 17, 2018

ENTASIS THERAPEUTICS LIMITED

CONSOLIDATED BALANCE SHEETS

(Amounts in thousands, except share and per-share amounts)

	December 31,	
	2016	**2017**
Assets		
Current assets:		
Cash and cash equivalents	$ 26,256	$ 55,101
Grants receivable	—	722
Due from related party	234	—
Prepaid expenses and other current assets	152	497
Total current assets	26,642	56,320
Property and equipment, net	364	646
Deferred offering costs	—	1,765
Other assets	63	63
Total assets	$ 27,069	$ 58,794
Liabilities, Redeemable Convertible Preference Shares and Shareholders' Deficit		
Current liabilities:		
Accounts payable	$ 898	$ 2,218
Due to related party	620	—
Accrued expenses	3,444	7,615
Total current liabilities	4,962	9,833
Deferred rent	34	38
Total liabilities	4,996	9,871
Commitments (Note 11)		
A redeemable convertible preference shares, nominal value of $1.00 per share; 33,499,900 shares issued and outstanding as of December 31, 2016 and 2017; liquidation and redemption value of $37,039 as of December 31, 2017	23,866	23,866
B redeemable convertible preference shares, nominal value of $1.00 per share; 25,000,000 shares issued and outstanding as of December 31, 2016 and 2017; liquidation and redemption value of $26,759 as of December, 31, 2017	24,550	24,550
B-1 redeemable convertible preference shares, nominal value of $0.59 per share; 0 and 96,440,678 shares issued and outstanding as of December 31, 2016 and 2017, respectively; liquidation and redemption value of $57,330 as of December 31, 2017	—	56,297
Shareholders' deficit:		
Ordinary shares, nominal value of $0.20 per share; 4 and 12,639 shares issued and outstanding as of December 31, 2016 and 2017, respectively	—	3
Additional paid-in capital	904	1,377
Accumulated deficit	(27,247)	(57,170)
Total shareholders' deficit	(26,343)	(55,790)
Total liabilities, redeemable convertible preference shares and shareholders' deficit	$ 27,069	$ 58,794

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

ENTASIS THERAPEUTICS LIMITED

CONSOLIDATED STATEMENTS OF OPERATIONS

(Amounts in thousands, except share and per-share amounts)

	Year Ended December 31,	
	2016	**2017**
Operating expenses:		
Research and development	$ 15,778	$ 25,745
General and administrative	3,326	5,599
Total operating expenses	19,104	31,344
Loss from operations	(19,104)	(31,344)
Other income:		
Grant income	—	1,396
Interest income	9	25
Total other income	9	1,421
Net loss	$ (19,095)	$ (29,923)
Net loss per share—basic and diluted	$(4,773,750.00)	$(13,795.76)
Weighted average ordinary shares outstanding—basic and diluted	4	2,169
Pro forma net loss per share—basic and diluted (unaudited)		$ (8.05)
Pro forma weighted average ordinary shares outstanding—basic and diluted (unaudited)		3,715,917

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

ENTASIS THERAPEUTICS LIMITED

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERENCE SHARES AND SHAREHOLDERS' DEFICIT

(Amounts in thousands, except share amounts)

	Redeemable Convertible Preference Shares						Ordinary Shares		Additional Paid-in Capital	Accumulated Deficit	Total Shareholders' Deficit
	A		B		B-1						
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Balances as of December 31, 2015	33,499,900	$23,866	—	$ —	—	$ —	4	$—	$ 334	$ (8,152)	$ (7,818)
Issuance of B redeemable convertible preference shares, net of issuance costs of $450	—	—	25,000,000	24,550	—	—	—	—	—	—	—
Share-based compensation expense	—	—	—	—	—	—	—	—	570	—	570
Net loss	—	—	—	—	—	—	—	—	—	(19,095)	(19,095)
Balances as of December 31, 2016	33,499,900	23,866	25,000,000	24,550	—	—	4	—	904	(27,247)	(26,343)
Issuance of B-1 redeemable convertible preference shares, net of issuance costs of $603	—	—	—	—	96,440,678	56,297	—	—	—	—	—
Exercise of share options	—	—	—	—	—	—	12,635	3	53	—	56
Share-based compensation expense	—	—	—	—	—	—	—	—	420	—	420
Net loss	—	—	—	—	—	—	—	—	—	(29,923)	(29,923)
Balances as of December 31, 2017	33,499,900	$23,866	25,000,000	$24,550	96,440,678	$56,297	12,639	$ 3	$1,377	$(57,170)	$(55,790)

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

ENTASIS THERAPEUTICS LIMITED

CONSOLIDATED STATEMENTS OF CASH FLOWS

(Amounts in thousands)

	Year Ended December 31,	
	2016	**2017**
Cash flows from operating activities:		
Net loss	$(19,095)	$(29,923)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	177	194
Share-based compensation expense	570	420
Changes in operating assets and liabilities:		
Grants receivable	—	(722)
Prepaid expenses and other assets	(170)	(345)
Accounts payable	641	447
Due to related party	—	(620)
Accrued expenses	1,907	3,386
Deferred rent	17	4
Net cash used in operating activities	(15,953)	(27,159)
Cash flows from investing activities:		
Purchases of property and equipment	(140)	(286)
Net cash used in investing activities	(140)	(286)
Cash flows from financing activities:		
Proceeds from issuance of redeemable convertible preference shares, net of issuance costs	42,192	56,531
Proceeds from share option exercises	—	56
Payments of initial public offering costs	—	(297)
Net cash provided by financing activities	42,192	56,290
Net increase in cash and cash equivalents	26,099	28,845
Cash and cash equivalents at beginning of period	157	26,256
Cash and cash equivalents at end of period	$ 26,256	$ 55,101
Supplemental disclosure of non-cash investing and financing activities:		
Purchases of property and equipment included in accounts payable	$ —	$ 190
Deferred offering costs included in accounts payable and accrued expenses	$ —	$ 1,468

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

1. Organization and Description of Business

Entasis Therapeutics Limited and subsidiary ("Entasis Ltd." 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 multi-drug resistant Gram-negative bacteria.

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

The Company is subject to risks common to other life science companies in the early development stage including, but not limited to, uncertainty of product development and commercialization, lack of marketing and sales history, development by its competitors of new technological innovations, dependence on key personnel, market acceptance of products, product liability, protection of proprietary technology, ability to raise additional financing and compliance with the Food and Drug Administration ("FDA") and other government regulations. If the Company does not successfully advance its programs into and through human clinical trials and/or enter into collaborations for its programs, and commercialize any of its product candidates, it may be unable to increase the value of the Company, produce product revenue or achieve profitability.

Going Concern

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

Through December 31, 2017, the Company has funded its operations primarily with proceeds from the sale of redeemable convertible preference shares. The Company has also either directly received funding or financial commitments from, or has had its program activities conducted and funded by, U.S. government agencies and non-profit entities. The Company has incurred recurring losses and negative operating cash flows from operations since its inception, including net losses of $19.1 million and $29.9 million for the years ended December 31, 2016 and 2017, respectively. In addition, the Company had an accumulated deficit of $57.2 million as of December 31, 2017. The Company expects to continue to generate operating losses for the foreseeable future.

As of March 23, 2018, the issuance date of these consolidated financial statements, the Company expects its cash and cash equivalents of $55.1 million as of December 31, 2017 will be sufficient to fund its operating expenses and capital expenditure requirements through December 2018. The future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its operations.

The Company is seeking to complete an initial public offering ("IPO") of its ordinary shares. In the event the Company does not complete an IPO, and even after the completion of an IPO, the

1. Organization and Description of Business (Continued)

Company expects to seek additional funding through equity financings, debt financings or other capital sources, including collaborations with other companies, government contracts or other strategic transactions. The Company may not be able to obtain financing on acceptable terms, or at all. The terms of any financing may adversely affect the holdings or the rights of the Company's shareholders.

If the Company is unable to obtain funding, the Company will be forced to delay, reduce or eliminate some or all of its drug development or future commercialization efforts, including its efforts for the advancement of its product candidates into and through human clinical trials, partnerships for its product candidates and platform, approval and commercialization of its products and technologies and achievement of profitability. Although management continues to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

Based on its recurring losses from operations incurred since inception, expectation of continuing operating losses for the foreseeable future, and the need to raise additional capital to finance future operations, the Company has concluded that there is substantial doubt about its ability to continue as a going concern within one year after the date that the consolidated financial statements are issued.

The accompanying consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty. Accordingly, the consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern and that contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

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 Ltd. (a U.K. corporation) and its wholly owned subsidiary Entasis Therapeutics Inc. (a U.S. corporation). The functional and reporting currency of the parent entity, Entasis Ltd., is U.S. Dollars. 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 expenses during the reporting period. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the recognition of research and development expenses and the valuation of ordinary shares and options to purchase ordinary shares. 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.

2. Summary of Significant Accounting Policies (Continued)

Cash and Cash Equivalents

All unrestricted highly liquid investments purchased with an original maturity date of 90 days or less at the date of purchase are considered to be cash equivalents.

The Company's cash equivalents, which are in a sweep account, are measured at fair value on a recurring basis. As of December 31, 2016 and 2017, the carrying amount of cash equivalents was $19.7 million and $3.3 million, respectively, which approximates fair value and was determined based upon Level 1 inputs. The sweep account is valued using quoted market prices with no valuation adjustments applied. Accordingly, these securities are categorized as Level 1.

Concentrations of Credit Risk and of Significant Suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash. 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 shareholders' 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. 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

2. Summary of Significant Accounting Policies (Continued)

Impairment of Long-Lived Assets

Long-lived assets, composed of property and equipment, to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, 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. To date, the Company has not recorded any impairment losses or disposals on long-lived assets.

Fair Value Measurements

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company does not have any assets or liabilities that are measured at fair value determined according to the fair value hierarchy described above as of December 31, 2016 and 2017 other than the sweep account described in the "Cash and Cash Equivalents" section above. The carrying values of the Company's cash equivalents, accounts payable and accrued expenses approximate their fair value due to their short-term nature.

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, 2016 and 2017, all of the Company's long-lived assets were domiciled in the United States.

2. Summary of Significant Accounting Policies (Continued)

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 qualifying expenses is recorded in the consolidated balance sheet as a liability. Grant income recognized upon incurring qualifying 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 ("G&A") expenses.

Share-Based Compensation

The Company measures share-based awards granted to employees and directors based on the estimated fair value of the award on the date of the grant and recognizes 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. The Company has issued share-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 share-based awards with performance-based vesting conditions.

For share-based awards granted to consultants and non-employees, compensation expense is recognized over the period during which services are rendered by such consultants and non-employees until completed. At the end of each financial reporting period prior to completion of the service, the

2. Summary of Significant Accounting Policies (Continued)

estimated fair value of these awards is remeasured using the then-current fair value of the Company's ordinary shares and updated assumption inputs in the Black-Scholes option-pricing model.

The Company classifies share-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 share option grant is estimated on the date of grant using the Black-Scholes option pricing model. The Company has been a private company and therefore lacks company-specific historical and implied volatility information for its shares. Therefore, the Company estimates its expected share 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 share price. The expected term of the Company's share options has been determined utilizing the "simplified" method. The "simplified" method estimates the expected term of share options as the mid-point between the weighted average time to vesting and the contractual maturity. The expected term of share options granted to non-employees is equal to the contractual term of the option award. 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 ordinary shares and does not expect to pay any cash dividends in the foreseeable future.

Income Taxes

The Company follows the asset and liability method of accounting for income taxes, as set forth in ASC 740, *Accounting for Income Taxes* ("ASC 740"). ASC 740 provides 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. Under ASC 740, 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 9 for further discussion of income taxes.

ASC 740-10, *Accounting for Uncertainty in Income Taxes* ("ASC 740-10"), provides detailed guidance for financial statement recognition, measurement and disclosure of uncertain tax positions recognized in an enterprise's financial statements. In accordance with ASC 740-10, income tax positions that meet a more-likely-than-not threshold are recognized. The Company recognizes potential accrued interest and penalties related to unrecognized tax benefits within the provision for income taxes. The Company has no liabilities recorded as of December 31, 2017 under ASC 740-10.

2. Summary of Significant Accounting Policies (Continued)

Net Loss Per Share

Basic and diluted net loss per ordinary share is determined by dividing net loss by the weighted-average ordinary shares outstanding during the period. For all periods presented, outstanding share options, A Preference Shares, B Preference Shares and B-1 redeemable convertible preference shares ("B-1 Preference Shares") 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.

Reverse Stock Split

In September 2018, the Company's board of directors and stockholders approved, and on September 17, 2018, 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 ordinary share and per share data included in the consolidated financial statements reflect the reverse stock split.

Unaudited Pro Forma Information

In the accompanying consolidated statements of operations, the unaudited pro forma basic and diluted net loss per share and the basic and diluted pro forma weighted average ordinary shares outstanding for the year ended December 31, 2017 have been prepared to give effect, upon the closing of a qualified IPO, to the automatic conversion of all outstanding redeemable convertible preference shares into ordinary shares as if they had been converted at the later of the beginning of the period or the date of issuance of the redeemable convertible preference shares.

Recently Adopted Accounting Pronouncements

In March 2016, the FASB issued ASU No. 2016-09, *Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"). The new standard involves several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities and classification on the statement of cash flows. Certain of these changes are required to be applied retrospectively, while other changes are required to be applied prospectively. ASU No. 2016-09 will be effective for fiscal years beginning after December 15, 2017, with early adoption permitted. The Company has elected to early adopt ASU 2016-09 and has reflected the adoption in its consolidated financial statements. The adoption of ASU 2016-09 had no impact on the Company's financial position, results of operations or cash flows.

In November 2015, the FASB issued ASU No. 2015-17, *Balance Sheet Classification of Deferred Taxes* ("ASU 2015-17"). ASU 2015-17 requires deferred tax liabilities and assets to be classified as non-current in the consolidated balance sheet. ASU 2015-17 is required to be adopted for annual periods beginning after December 15, 2016, including interim periods within those fiscal years. The amendment may be applied either prospectively to all deferred tax liabilities and assets or retrospectively to all periods presented. The Company has elected to early adopt ASU 2015-17 and has reflected the adoption in its consolidated financial statements. The adoption of ASU 2015-17 did not have a material impact on the Company's financial position, results of operations or cash flows.

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern* (Subtopic 205-40) ("ASU 2014-15"). The amendments in this

2. Summary of Significant Accounting Policies (Continued)

update explicitly require a company's management to assess an entity's ability to continue as a going concern and to provide related footnote disclosures in certain circumstances. The new standard is effective in the first annual period ending after December 15, 2016. The Company adopted ASU 2014-15 and has provided the related footnote disclosure.

Recently Issued Accounting Pronouncements

In July 2017, the FASB issued ASU No. 2017-11, *Earnings Per Share (Topic 260); Distinguishing Liabilities from Equity (Topic 480); Derivatives and Hedging (Topic 815): (Part I) Accounting for Certain Financial Instruments with Down Round Features, (Part II) Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception* ("ASU 2017-11"). Part I of this update addresses the complexity of accounting for certain financial instruments with down round features. Down round features are features of certain equity-linked instruments (or embedded features) that result in the strike price being reduced on the basis of the pricing of future equity offerings. Current accounting guidance creates cost and complexity for entities that issue financial instruments (such as warrants and convertible instruments) with down round features that require fair value measurement of the entire instrument or conversion option. Part II of this update addresses the difficulty of navigating Topic 480, Distinguishing Liabilities from Equity, because of the existence of extensive pending content in the FASB Accounting Standards Codification. This pending content is the result of the indefinite deferral of accounting requirements about mandatorily redeemable financial instruments of certain nonpublic entities and certain mandatorily redeemable noncontrolling interests. The amendments in Part II of this update do not have an accounting effect. ASU 2017-11 is effective for fiscal years beginning after December 15, 2018 and interim periods within those years. The Company is currently evaluating the impact that the adoption of ASU 2017-11 will have on its consolidated financial statements.

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, including interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the impact that the adoption of ASU 2017-09 will have on its consolidated financial statements

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. The Company is currently evaluating the impact that the adoption of ASU 2016-16 will have on its consolidated financial statements.

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

2. Summary of Significant Accounting Policies (Continued)

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. Early adoption is permitted. The adoption of ASU 2016-15 is required to be applied retrospectively. The Company is currently evaluating the impact that the adoption of ASU 2016-15 will have on its consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* ("ASU 2016-02"), which applies to all leases and will require lessees to record most leases on the balance sheet, but recognize expense in a manner similar to the current standard. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018 and interim periods within those years. Entities are required to use a modified retrospective approach of adoption for leases that exist or are entered into after the beginning of the earliest comparative period in the financial statements. Full retrospective application is prohibited. The Company is currently evaluating the impact that the adoption of ASU 2016-02 will have on its consolidated financial statements.

In May 2014, the FASB issued 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 adoption of these standards is not expected to have an impact on the Company's financial position, results of operations or cash flows as the Company does not currently have any revenue generating arrangements.

3. Property and Equipment, Net

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

	December 31,	
	2016	2017
Laboratory equipment	$ 575	$1,036
Computer software	63	71
Computer equipment	—	7
Total	638	1,114
Less: Accumulated depreciation	(274)	(468)
Property and equipment, net	$ 364	$ 646

Depreciation expense was $0.2 million for each of the years ended December 31, 2016 and 2017.

4. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2016	2017
Accrued compensation and benefits	$1,073	$1,286
Accrued contract manufacturing	1,789	3,633
Accrued clinical trial costs	302	1,096
Accrued professional services	140	1,246
Other	140	354
Total accrued expenses	$3,444	$7,615

5. 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 December 2018 (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.

As of December 31, 2017, no funding had been received and the Company had incurred $0.5 million of specified expenses under the USAMRAA grant. As of December 31, 2017, the Company recorded a receivable of $0.5 million to reflect unreimbursed, eligible costs incurred under the grant. Grant income of $0.5 million was recognized for the year ended December 31, 2017.

In March 2017 and October 2017, the Company entered into funding agreements 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 agreements will cover up to $16.4 million of specified research expenditures of the Company from April 2017 through September 2021.

5. Funding Arrangements (Continued)

The Company recognized $0.9 million of grant income for the year ended December 31, 2017 in connection with the CARB-X agreements. As of December 31, 2017, the Company recorded a receivable of $0.2 million to reflect unreimbursed, eligible costs incurred under the grant.

Collaboration Agreement

In July 2017, the Company entered into a collaboration agreement (the "Agreement") with the Drugs for Neglected Disease initiative ("DNDi") for the development, manufacture and commercialization of a product candidate containing zoliflodacin in certain countries.

Under the Agreement, DNDi will fully fund the Phase 3 clinical trial, including the manufacture and supply of the product candidate containing zoliflodacin, in uncomplicated gonorrhea. The Phase 3 clinical trial had not commenced as of December 31, 2017. Outside of the funding of the Phase 3 clinical trial, the Agreement does not include any arrangement consideration or cost reimbursement provisions between the Company and DNDi except for instances in which the Company incurs costs and expenses for the maintenance of patent rights in what has been determined to be DNDi territory, in which case DNDi will reimburse the Company. The Company expenses patent costs as incurred and records such costs within G&A expenses. Reimbursement payments received from DNDi are recognized as a reduction to G&A expense. During 2017, the Company incurred $5,000 of patent costs reimbursable under the Agreement and had not received any funding as of December 31, 2017.

6. Redeemable Convertible Preference Shares

As of each balance sheet date, the redeemable convertible preference shares consisted of the following (in thousands, except share amounts):

	December 31, 2016			
	Preference Shares Issued and Outstanding	Carrying Value	Liquidation and Redemption Value	Ordinary Shares Issuable Upon Conversion
A preference shares	33,499,900	$23,866	$35,699	1,616,166
B preference shares	25,000,000	24,550	25,759	1,206,096
	58,499,900	$48,416	$61,458	2,822,262

	December 31, 2017			
	Preference Shares Issued and Outstanding	Carrying Value	Liquidation and Redemption Value	Ordinary shares Issuable Upon Conversion
A preference shares	33,499,900	$ 23,866	$ 37,039	1,616,166
B preference shares	25,000,000	24,550	26,759	1,206,096
B-1 preference shares	96,440,678	56,297	57,330	4,652,668
	154,940,578	$104,713	$121,128	7,474,930

The Company's amended and restated articles of association authorized the Company to issue redeemable convertible preference shares as part of the rights granted to the board of directors to subscribe for or convert any security into shares of the Company, up to a maximum nominal value of

6. Redeemable Convertible Preference Shares (Continued)

$125.0 million as of December 31, 2017. The authorization is for any class of shares, including ordinary shares, and the nominal value noted is based on the nominal value of each share. As of December 31, 2017, the Company was authorized to subscribe for, or convert securities into, shares of the Company, up to a remaining nominal value of $6.2 million after considering the issued and outstanding redeemable convertible preference shares, ordinary shares and options outstanding. The redeemable convertible preference shares are classified outside of shareholders' equity (deficit) because the shares contain certain redemption features that are not solely within the control of the Company.

In May 2015, the Company entered into a Business Transfer and Subscription Agreement (the "A Subscription Agreement") with AstraZeneca as the sole investor. Under the terms of the A Subscription Agreement, the Company sold 33,499,900 A Preference Shares with a nominal value of $1.00 per share to AstraZeneca in consideration for property and equipment, clinical materials, intellectual property and net cash proceeds of $23.3 million, of which $17.6 million and $0.2 million of the cash proceeds were received during the years ended December 31, 2016 and 2017, respectively.

In March 2016, the Company entered into the Entasis Therapeutics Limited B Preference Share Subscription Agreement (the "B Subscription Agreement"). Under the terms of the B Subscription Agreement, the Company issued 25,000,000 B Preference Shares at $1.00 per share for net proceeds of $24.6 million. As of December 31, 2016 under the B Subscription Agreement, if the Company achieved certain milestones by December 31, 2017, the same investors had the option to purchase an additional 25,000,000 B Preference Shares for $1.00 per share. Regardless of the Company achieving such milestones, the investors also had the option, by written notice signed by a majority of the board of directors and holders of the B Preference Shares, to elect to purchase such shares by December 31, 2017.

In August 2017, the Company entered into a subscription agreement for B-1 Preference Shares (the "B-1 Subscription Agreement"). In connection with this transaction, the B Preference Share investors no longer had the option to purchase an additional 25,000,000 B Preference Shares if the Company achieved certain milestones by December 31, 2017. Under the terms of the B-1 Subscription Agreement, the Company issued 42,372,882 B-1 Preference Shares at $0.59 per share for net proceeds of $24.4 million. Per the B-1 Subscription Agreement, the Company was required to issue and allot an additional 54,067,796 B-1 Preferences Shares at $0.59 per share upon an issuance trigger event ("ITE").

In December 2017, the board of directors and a majority of the holders of the B-1 Preference Shares elected to accelerate the ITE and issued the additional 54,067,796 B-1 Preference Shares at $0.59 per share for net proceeds of $31.9 million, allocated among the investors in the same proportions as the initial issuance of the B-1 Preference Shares.

The holders of the A Preference Shares, B Preference Shares and B-1 Preference Shares (collectively, the "Preference Shares") have the following rights and preferences:

Voting Rights

The Preference Shares shall have one vote for each ordinary share into which the Preference Share is convertible on a one-to-one basis. Preference Shares and ordinary shares vote together as a single class.

In the event that the A Preference Shares would constitute greater than 50% of the ordinary shares (on an as-converted basis), then the A Preference Shares, as a class, shall have votes equal to

6. Redeemable Convertible Preference Shares (Continued)

49% of the ordinary shares (on an as-converted basis) and the voting rights attaching to each of the A Preference Shares shall accordingly be reduced on a pro-rata basis.

Distributions

The holders of Preference Shares are entitled to receive a cumulative preferential dividend at a fixed rate of 4.0% of the issuance price annually. Cumulative dividends for A Preference Shares, B Preference Shares and B-1 Preference Shares were $3.5 million, $1.8 million and $0.4 million as of December 31, 2017, respectively. No dividends have been declared by the Company's board of directors, and management has determined that it is not probable the Company will pay dividends, whether by the board of directors' declaration or a liquidation event. Therefore, the Company had not accrued any dividends payable as of December 31, 2017.

Liquidation Preference

In the event of a Deemed Liquidation Event (as defined below), holders of the B-1 Preference Shares then outstanding will be 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 Preference Shares, A Preference Shares and ordinary shareholders or (b) the amount per share as would have been payable to the holders of the B-1 Preference Shares had the conversion of the B-1 Preference Shares into ordinary shares taken place immediately prior to the date of the Deemed Liquidation Event (taking into account the conversion of all series of the Preference Shares simultaneously).

Next, the holders of the B Preference Shares then outstanding will 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 Preference Shares and ordinary shareholders or (b) the amount per share as would have been payable to the holders of the B Preference Shares had the conversion of the B Preference Shares into ordinary shares taken place immediately prior to the date of the Deemed Liquidation Event (taking into account the conversion of all series of the Preference Shares simultaneously).

Next, the holders of the A Preference Shares then outstanding will 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 ordinary shareholders or (b) the amount per share as would have been payable to the holders of the A Preference Shares had the conversion of the A Preference Shares into ordinary shares taken place immediately prior to the date of the Deemed Liquidation Event (taking into account the conversion of all series of Preference Shares simultaneously).

After payment to the holders of the Preference Shares, any remaining assets of the Company available for distribution to its shareholders shall be distributed among the ordinary shareholders pro rata based on the number of shares held by each such holder.

A Deemed Liquidation Event is 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

6. Redeemable Convertible Preference Shares (Continued)

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 Preference Shares shall have the following rights with respect to the conversion into ordinary shares:

- The Preference Shares are convertible at the option of the holder, at any time into ordinary shares on a one-for-20.728 basis. These rights terminate in the event of a change in control, Deemed Liquidation Event, or termination by the Company without cause.
- All Preference Shares are automatically converted into ordinary shares 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 Preference Shares; (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 Preference Shares.

Redemption

The Preference Shares are redeemable upon the occurrence of a Deemed Liquidation Event, which is not solely in control of the Company. Therefore, the Preference Shares have been classified as temporary equity.

7. Ordinary Shares

The voting and liquidation rights of the holders of the Company's ordinary shares are subject to and qualified by the rights, powers and preferences of the holders of the Preference Shares set forth above. Ordinary shareholders are entitled to receive dividends, as may be declared by the board of directors, if any, subject to the preferential dividend rights of the Preference Shares. Through December 31, 2017, no cash dividends have been declared or paid.

In May 2015, in conjunction with the spin-out of the Company, the Company issued 4 ordinary shares to AstraZeneca. The ordinary shares have a nominal value of $0.20 per share and there were 4 and 12,639 ordinary shares issued and outstanding as of December 31, 2016 and 2017, respectively.

8. Share-Based Compensation

Entasis Therapeutics Limited 2015 Share Incentive Plan

The Company maintains the Entasis Therapeutics Limited 2015 Share Incentive Plan (the "2015 Plan") for the benefit of certain of its officers, employees, non-employee directors and other key persons (including consultants and advisory board members). All options and awards granted under the 2015 Plan consist of the Company's ordinary shares. The maximum number of ordinary shares that may be issued under the 2015 Plan as of December 31, 2017 was 1,267,680, of which 443,417 were available to grant.

8. Share-Based Compensation (Continued)

The 2015 Plan is administered by the board of directors of the Company. The exercise prices, vesting periods and other restrictions are determined at the discretion of the board of directors, except that the exercise price per share of options may not be less than 100% of the fair value of the ordinary shares on the date of grant. Options granted to employees generally vest over four years with 25% vesting on the first annual anniversary date and the remainder on a monthly basis for the remaining three years. Some options granted to non-employees vest within one year. The contractual life of the options is 10 years.

During the years ended December 31, 2016 and 2017, the Company granted options to employees and directors to purchase 181,029 and 436,493 ordinary shares, respectively. The Company recorded share-based compensation expense for options granted to employees and directors of $0.2 million and $0.3 million during the years ended December 31, 2016 and 2017, respectively.

During the years ended December 31, 2016 and 2017, the Company granted options to non-employees to purchase 8,443 and 9,948 ordinary shares, respectively. The Company recorded share-based compensation expense for options granted to non-employees of $10,000 and $0.1 million during the years ended December 31, 2016 and 2017, respectively.

The following table summarizes the Company's option activity under the 2015 Plan for the year ended December 31, 2017:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2016	401,108	$4.39	9.19	$ —
Granted	446,441	3.19	9.84	
Exercised	(12,635)	4.47		—
Cancelled or forfeited	(23,287)	4.39		
Outstanding as of December 31, 2017	811,627	$3.73	9.09	$6,062
Options exercisable as of December 31, 2017	197,627	$4.51	8.08	$1,323
Options unvested as of December 31, 2017	614,000	$3.48	9.42	$4,740

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 ordinary shares for those options that had exercise prices lower than the fair value of the Company's ordinary shares.

The weighted average grant-date fair value per share of options granted during the years ended December 31, 2016 and 2017 was $2.10 and $3.75 per share, respectively. The total fair value of options vested during the years ended December 31, 2016 and 2017 was $0.2 million and $0.3 million, respectively.

8. Share-Based Compensation (Continued)

The assumptions that the Company used to determine the grant-date fair value of options granted to employees and directors were as follows, presented on a weighted average basis:

	Year Ended December 31,	
	2016	2017
Weighted average risk-free interest rate	1.39%	2.16%
Expected term (in years)	6.10	6.08
Expected volatility	60.50%	65.62%
Expected dividend yield	0.00%	0.00%
Weighted average fair value of ordinary shares	$3.74	$5.38

AstraZeneca Shares Option and Incentive Plan

Certain employees of the Company participate 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 vest 100% after 36 months and were fully vested in March 2017.

The Company recorded share-based compensation expense for AstraZeneca RSUs of $0.4 million and $15,000 during the years ended December 31, 2016 and 2017, respectively, included in the table presented below. The Company's compensation expense related to the AstraZeneca RSUs is based on the fair value of AstraZeneca's ordinary shares as of the date of the issuance to the employees during their employment at AstraZeneca. Because the employees were employees of the consolidated group at the time of the spin-out of the Company and were providing services to the Company, the Company began recognizing the remaining compensation expense. When AstraZeneca no longer held a controlling interest in the Company, the Company became an equity method investment of AstraZeneca. Accordingly, the Company began recognizing the remaining compensation expense as non-employee awards over the remainder of the requisite service period as those employees were no longer employees of AstraZeneca.

Share-Based Compensation

Share-based compensation expense was classified in the consolidated statement of operations as follows (in thousands):

	Year Ended December 31,	
	2016	2017
Research and development	$202	$229
General and administrative	368	191
	$570	$420

As of December 31, 2017, total unrecognized compensation expense related to the unvested options was $2.0 million, which is expected to be recognized over the weighted average period of approximately 2.8 years.

9. Income Taxes

During the years ended December 31, 2016 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. The Company's losses before income taxes were generated in the United States and the United Kingdom.

Net loss before the provision for income taxes for the years ended December 31, 2016 and 2017, consisted of the following (in thousands):

	Year Ended December 31,	
	2016	2017
United Kingdom	$13,410	$21,806
United States	5,685	8,117
	$19,095	$29,923

A reconciliation of the federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2016	2017
Income tax benefit computed at U.K. statutory tax rate	20.0%	19.0%
State taxes, net of federal benefit	1.3	1.3
Foreign rate differential	4.2	4.1
Research and development tax credits	3.0	3.0
Permanent difference	(1.0)	(1.3)
Valuation allowances	(27.5)	(17.7)
Rate changes	—	(8.4)
Effective income tax rate	0.0%	0.0%

Net deferred tax assets as of December 31, 2016 and 2017 consisted of the following (in thousands):

	December 31,	
	2016	2017
Deferred tax assets:		
Net operating loss carryforwards	$ 4,924	$ 8,967
Tax credit carryforwards	806	1,763
Depreciation and amortization	—	7
Accrued expenses and other	689	987
Total deferred tax assets	6,419	11,724
Depreciation and amortization	(4)	—
Total deferred tax liabilities	(4)	—
Valuation allowance	(6,415)	(11,724)
Net deferred tax assets	$ —	$ —

9. Income Taxes (Continued)

On December 22, 2017, the President of the United States signed into law the Tax Cuts and Jobs Act 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 enacted law, the Company has 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.

As of December 31, 2017, the Company had U.S. federal and state net operating loss carryforwards ("NOLs") of $10.8 million and $11.1 million, respectively, which begin to expire in 2035. As of December 31, 2017, the Company had federal and state research and development tax credits carryforwards of $1.3 million and $0.6 million, which begin to expire in 2035 and 2030, 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, 2017, the Company had NOLs in the United Kingdom of $35.2 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 $11.7 million has been established against the deferred tax assets as of December 31, 2017.

9. Income Taxes (Continued)

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2016 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,	
	2016	2017
Valuation allowance at beginning of year	$(1,183)	$ (6,415)
Increases recorded to income tax provision	(5,232)	(5,309)
Valuation allowance at end of year	$(6,415)	$(11,724)

The Company has not recorded an amount for unrecognized tax benefits or related interest and penalties accrued as of December 31, 2017. 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.

10. Net Loss per Share

Basic and diluted net loss per share was calculated as follows (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2016	2017
Numerator:		
Net loss	$ (19,095)	$ (29,923)
Denominator:		
Weighted average ordinary shares outstanding—basic and diluted	4	2,169
Net loss per share—basic and diluted	$(4,773,750.00)	$(13,795.76)

The Company excluded the following potential ordinary shares, 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

10. Net Loss per Share (Continued)

average number of ordinary shares outstanding used to calculate both basic and diluted net loss per share is the same.

	As of December 31,	
	2016	2017
Options to purchase ordinary shares	401,108	811,627
Redeemable convertible preference shares (as converted to ordinary shares)	2,822,262	7,474,930
	3,223,370	8,286,557

11. Commitments

Lease Commitments

The Company has an operating lease agreement for its office and laboratory space with AstraZeneca, which extends through May 2020 and includes certain renewal periods. The facility lease requires the Company to pay certain operating costs. Rental expense was $0.4 million for each of the years ended December 31, 2016 and 2017.

Future minimum lease payments as of December 31, 2017 were as follows (in thousands):

Year Ending December 31,	
2018	$389
2019	402
2020	146
	$937

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 ordinary shares 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, ordinary shares, or a combination of cash and ordinary shares. Additionally, the Company is obligated to pay AstraZeneca tiered, single-digit, per-country royalties on the annual worldwide net sales of ETX2514 and zoliflodacin.

12. 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 Preference Shares were issued in March 2016. As of December 31, 2017, AstraZeneca was the sole A Preference Shareholder.

12. Related Party Transactions (Continued)

Subscription Receivable Due from AstraZeneca

In connection with the issuance and sale of A Preference Shares, AstraZeneca agreed to provide cash management services for the net proceeds due to the Company under the A Preference Shares 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 Preference Shares 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 11.

Share-Based Compensation

Certain employees of the Company continue to vest in restricted shares of AstraZeneca through an incentive plan. See Note 8.

AstraZeneca Transition Services Agreement

The Company and AstraZeneca entered into a transition services agreement (the "Transition Agreement"), which commenced on May 11, 2015 and expired in November 2015. The Company owed $0.6 million as of December 31, 2016 related to this arrangement, included in due to related party on the consolidated balance sheet, which it paid during the year ended December 31, 2017.

13. 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 $0.1 million for each of the years ended December 31, 2016 and 2017.

14. Subsequent Events

The Company evaluated subsequent events through March 23, 2018, the date on which these consolidated financial statements were issued.

Lease Extension

In January 2018, the Company amended its operating lease agreement, effective February 2, 2018, for its office and laboratory space with AstraZeneca. The amendment extends the lease term through December 31, 2022, and expands the premises to include an additional 7,257 square feet beginning on

14. Subsequent Events (Continued)

February 2, 2018. Future minimum lease payments for the combined space will be as follows (in thousands):

Year Ending December 31,	
2018	$ 472
2019	597
2020	656
2021	710
2022	730
	$3,165

ENTASIS THERAPEUTICS HOLDINGS INC.

CONSOLIDATED BALANCE SHEETS

(Unaudited, amounts in thousands, except share and per-share amounts)

	December 31, 2017	June 30, 2018	Pro Forma June 30, 2018
Assets			
Current assets:			
Cash and cash equivalents	$ 55,101	$ 33,643	$ 33,643
Grants receivable	722	2,560	2,560
Prepaid expenses and other current assets	497	1,902	1,902
Total current assets	56,320	38,105	38,105
Property and equipment, net	646	620	620
Deferred offering costs	1,765	2,715	2,715
Other assets	63	63	63
Total assets	$ 58,794	$ 41,503	$ 41,503
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)			
Current liabilities:			
Accounts payable	$ 2,218	$ 2,044	$ 2,044
Accrued expenses	7,615	6,343	6,343
Total current liabilities	9,833	8,387	8,387
Deferred rent	38	120	120
Total liabilities	9,871	8,507	8,507
Commitments (Note 7)			
Series A redeemable convertible preferred stock, par value $0.001; 33,499,900 shares authorized, issued and outstanding as of December 31, 2017 and June 30, 2018; liquidation and redemption value of $37,703 as of June 30, 2018	23,866	23,866	—
Series B redeemable convertible preferred stock, par value $0.001; 25,000,000 shares authorized, issued and outstanding as of December 31, 2017 and June 30, 2018; liquidation and redemption value of $27,255 as of June 30, 2018	24,550	24,550	—
Series B-1 Tranche A redeemable convertible preferred stock, par value $0.001; 42,372,882 shares authorized, issued and outstanding as of December 31, 2017 and June 30, 2018; liquidation and redemption value of $25,838 as of June 30, 2018	24,423	24,423	—
Series B-1 Tranche B redeemable convertible preferred stock, par value $0.001; 54,067,796 shares authorized, issued and outstanding as of December 31, 2017 and June 30, 2018; liquidation and redemption value of $32,620 as of June 30, 2018	31,874	31,874	—
Stockholders' equity (deficit):			
Common stock, par value $0.001; 250,000,000 shares authorized; 12,639 shares issued and outstanding as of December 31, 2017 and June 30, 2018; 125,000,000 shares authorized and 8,005,261 shares issued and outstanding, pro forma as of June 30, 2018	3	—	8
Additional paid-in capital	1,377	1,840	106,545
Accumulated deficit	(57,170)	(73,557)	(73,557)
Total stockholders' equity (deficit)	(55,790)	(71,717)	32,996
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 58,794	$ 41,503	$ 41,503

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

ENTASIS THERAPEUTICS HOLDINGS INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

(Unaudited, amounts in thousands, except per share amounts)

	Six Months Ended June 30,	
	2017	**2018**
Revenue	$ —	$ 5,000
Operating expenses:		
Research and development	10,828	18,029
General and administrative	2,103	5,766
Total operating expenses	12,931	23,795
Loss from operations	(12,931)	(18,795)
Other income:		
Grant income	491	2,839
Interest income	12	28
Total other income	503	2,867
Loss before income taxes	(12,428)	(15,928)
Provision for income taxes	—	472
Net loss	$ (12,428)	$ (16,400)
Net loss per share—basic and diluted	$(30,092.01)	$ (1,297.57)
Weighted average shares outstanding—basic and diluted	413	12,639
Pro forma net loss per share—basic and diluted		$ (2.19)
Pro forma weighted average shares outstanding—basic and diluted		7,487,569

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

ENTASIS THERAPEUTICS HOLDINGS INC.

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT

(Unaudited, amounts in thousands, except share amounts)

	Redeemable Convertible Preferred Stock								Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Deficit
	A		B		B-1 A		B-1 B						
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
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	—	—	—	—	—	—	—	—	—	—	473	—	473
Reorganization adjustment	—	—	—	—	—	—	—	—	—	(3)	3	—	—
Net loss	—	—	—	—	—	—	—	—	—	—	—	(16,400)	(16,400)
Balances as of June 30, 2018	33,499,900	$23,866	25,000,000	$24,550	42,372,882	$24,423	54,067,796	$31,874	12,639	$—	$1,840	$(73,557)	$(71,717)

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

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

	Six Months Ended June 30,	
	2017	**2018**
Cash flows from operating activities:		
Net loss	$(12,428)	$(16,400)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	97	89
Stock-based compensation expense	205	473
Changes in operating assets and liabilities:		
Grants receivable	(463)	(1,838)
Prepaid expenses and other assets	(368)	(1,405)
Accounts payable	(290)	678
Due to related party	(620)	—
Accrued expenses	348	(845)
Deferred rent	4	82
Net cash used in operating activities	(13,515)	(19,166)
Cash flows from investing activities:		
Purchases of property and equipment	(5)	(253)
Net cash used in investing activities	(5)	(253)
Cash flows from financing activities:		
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	234	—
Proceeds from exercise of stock options	5	—
Payments of initial public offering costs	—	(2,039)
Net cash provided by (used in) financing activities	239	(2,039)
Net decrease in cash and cash equivalents	(13,281)	(21,458)
Cash and cash equivalents at beginning of period	26,256	55,101
Cash and cash equivalents at end of period	$ 12,975	$ 33,643
Supplemental disclosure of non-cash investing and financing activities:		
Deferred initial public offering costs included in accounts payable and accrued expenses	$ —	$ 378

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

ENTASIS THERAPEUTICS HOLDINGS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(Unaudited)

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 multi-drug resistant Gram-negative bacteria.

The Company was initially formed as Entasis Therapeutics Limited ("Entasis Limited") on March 6, 2015 in the United Kingdom 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, 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. 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. 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.

The Company is subject to risks common to other life science companies in the early development stage including, but not limited to, uncertainty of product development and commercialization, lack of marketing and sales history, development by its competitors of new technological innovations, dependence on key personnel, market acceptance of products, product liability, protection of proprietary technology, ability to raise additional financing and compliance with the Food and Drug Administration ("FDA") and other government regulations. If the Company does not successfully advance its programs into and through human clinical trials and/or enter into collaborations for its programs, and commercialize any of its product candidates, it may be unable to increase the value of the Company, produce product revenue or achieve profitability.

1. Organization and Description of Business (Continued)

Going Concern

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

Through June 30, 2018, the Company has funded its operations primarily with proceeds from the sale of redeemable convertible preferred stock. The Company has also either directly received funding or financial commitments from, or has had its program activities conducted and funded by, U.S. government agencies and non-profit entities. The Company has incurred recurring losses and negative operating cash flows from operations since its inception, including a net loss of $16.4 million for the six months ended June 30, 2018. In addition, the Company had an accumulated deficit of $73.6 million as of June 30, 2018. The Company expects to continue to generate operating losses for the foreseeable future.

As of August 17, 2018, the issuance date of these consolidated financial statements, the Company expects its cash and cash equivalents of $33.6 million as of June 30, 2018 will be sufficient to fund its operating expenses and capital expenditure requirements through March 2019. The future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its operations.

The Company is seeking to complete an initial public offering ("IPO") of its shares of common stock. In the event the Company does not complete an IPO, and even after the completion of an IPO, the Company expects to seek additional funding through equity financings, debt financings or other capital sources, including collaborations with other companies, government contracts or other strategic transactions. The Company may not be able to obtain financing on acceptable terms, or at all. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders.

If the Company is unable to obtain funding, the Company will be forced to delay, reduce or eliminate some or all of its drug development or future commercialization efforts, including its efforts for the advancement of its product candidates into and through human clinical trials, partnerships for its product candidates and platform, approval and commercialization of its products and technologies and achievement of profitability. Although management continues to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

Based on its recurring losses from operations incurred since inception, expectation of continuing operating losses for the foreseeable future, and need to raise additional capital to finance future operations, the Company has concluded that there is substantial doubt about its ability to continue as a going concern within one year after the date that the unaudited consolidated financial statements are issued.

The accompanying consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty. Accordingly, the unaudited consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern

1. Organization and Description of Business (Continued)

and which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

2. Summary of Significant Accounting Policies

Significant Accounting Policies

The Company's significant accounting policies are disclosed in the audited consolidated financial statements for the year ended December 31, 2017, included elsewhere in this prospectus. Since the date of those financial statements, there have been no changes to its significant accounting policies other than those noted below.

Basis of Presentation and Consolidation

The accompanying consolidated balance sheet as of June 30, 2018 and the consolidated statements of operations, redeemable convertible preferred stock and stockholders' deficit and cash flows for the six months ended June 30, 2017 and 2018 are unaudited. The interim unaudited consolidated financial statements have been prepared on the same basis as the annual audited consolidated financial statements; and in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for the fair statement of the Company's financial position as of June 30, 2018 and the results of operations, comprehensive loss, and cash flows for the six months ended June 30, 2017 and 2018. The financial data and other information disclosed in these notes as of June 30, 2017 and 2018 are unaudited. The results for the six months ended June 30, 2018 are not necessarily indicative of the results to be expected for the year ending December 31, 2018, any other interim periods, or any future year or period. The consolidated financial statements include the accounts of Entasis Therapeutics Holdings Inc. and its wholly owned subsidiaries Entasis Limited (a U.K. corporation) and Entasis Therapeutics Inc. (a U.S. corporation). The functional and reporting currency of the parent entity, Entasis Therapeutics Holdings Inc., is U.S. Dollars. 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 and options to purchase common stock. 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.

2. Summary of Significant Accounting Policies (Continued)

Revenue Recognition

The Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition, 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. See Note 5 for a further discussion of accounting for revenue.

Reverse Stock Split

In September 2018, the Company's board of directors and stockholders approved, and on September 17, 2018, 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.

Unaudited Pro Forma Information

The accompanying unaudited pro forma consolidated balance sheet as of June 30, 2018 has been prepared to give effect, upon the closing of a qualified IPO, to the automatic conversion of all outstanding redeemable convertible preferred stock, including the accrued dividends as of August 31, 2018, into 7,992,622 shares of common stock.

In the accompanying consolidated statements of operations, the unaudited pro forma basic and diluted net loss per share and the basic and diluted pro forma weighted average shares outstanding for the six months ended June 30, 2018 have been prepared to give effect, upon the closing of a qualified IPO, to the automatic conversion of all outstanding redeemable convertible preferred stock into shares of common stock as if they had been converted at the later of the beginning of the period or the date of issuance of the redeemable convertible preferred stock.

Recently Adopted Accounting Pronouncements

In May 2014, the FASB issued 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*

2. Summary of Significant Accounting Policies (Continued)

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. See Note 5. 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 unaudited 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 unaudited 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.

2. Summary of Significant Accounting Policies (Continued)

In June 2018, the FASB issued ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("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 six months ended June 30, 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.

3. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31, 2017	June 30, 2018
Accrued compensation and benefits	$1,286	$ 954
Accrued contract manufacturing	3,633	3,548
Accrued clinical trial costs	1,096	572
Accrued professional services	1,246	701
Other	354	568
Total accrued expenses	$7,615	$6,343

4. 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 December 2018 (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 $0.3 million for both of the six months ended June 30, 2017 and 2018. The Company received $0.6 million of funding under the grant for the six months ended June 30, 2018. The Company did not receive any funding under the grant during the six months ended June 30, 2017. As of June 30, 2018, the Company recorded a receivable of $0.2 million to reflect unreimbursed, eligible costs incurred under the grant.

In March 2017 and October 2017, the Company entered into funding agreements 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 agreements will cover up to $16.4 million of specified research expenditures of the Company from April 2017 through September 2021.

4. Funding Arrangements (Continued)

The Company recognized $2.5 million and $0.2 million of grant income for the six months ended June 30, 2018 and 2017, respectively, in connection with the CARB-X agreements. As of June 30, 2018, the Company recorded a receivable of $2.4 million to reflect unreimbursed, eligible costs incurred under the CARB-X agreements.

Collaboration Agreement

In July 2017, the Company entered into a collaboration agreement (the "Agreement") with the Drugs for Neglected Disease Initiative ("DNDi") 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 June 30, 2018.

5. 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. Under the terms of the 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, from Zai Lab and the Company is eligible to receive up to an aggregate of $98.6 million in 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

5. License and Collaboration Agreement with Zai Lab (Continued)

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.

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

6. Stock-Based Compensation

2015 Stock Incentive Plan

The Company maintains the Entasis Therapeutics Holdings Inc. 2015 Stock Incentive Plan (the "2015 Plan") for the benefit of certain of its officers, employees, non-employee directors and other key persons (including consultants and advisory board members). All options and awards granted under the 2015 Plan consist of the Company's common stock. The maximum number of shares of common stock that may be issued under the 2015 Plan as of June 30, 2018 was 1,267,680, of which 86,107 were available to grant, as of June 30, 2018.

The 2015 Plan is administered by the board of directors of the Company. The exercise prices, vesting periods and other restrictions are determined at the discretion of the board of directors, except that the exercise price per share of options may not be less than 100% of the fair value of the Company's common stock on the date of grant. Options granted to employees generally vest over four years with 25% vesting on the first annual anniversary date and the remainder on a monthly basis for the remaining three years. Some options granted to non-employees vest within one year. The contractual life of the options is 10 years.

During the six months ended June 30, 2018, 363,243 options were granted by the Company to employees and directors or non-employees.

6. Stock-Based Compensation (Continued)

The following table summarizes the Company's option activity under the 2015 Plan for the six months ended June 30, 2018:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2017	811,627	$3.73	9.09	$6,062
Granted	363,243	6.85		
Cancelled or forfeited	(5,932)	3.30		
Outstanding as of June 30, 2018	1,168,938	$4.70	8.98	$2,508
Options exercisable as of June 30, 2018	257,514	$4.45	7.68	$ 619
Options unvested as of June 30, 2018	911,424	$4.78	9.35	$1,889

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.

The weighted average grant-date fair value per share of options granted during the six months ended June 30, 2018 was $4.15 per share. The total fair value of options vested during the six months ended June 30, 2018 was $0.3 million.

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 vested 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 June 30, 2017. The Company recorded stock-based compensation expense for AstraZeneca RSUs of $14,604 during the six months ended June 30, 2017.

Stock-Based Compensation

Stock-based compensation expense was classified in the consolidated statement of operations as follows (in thousands):

	Six Months Ended June 30,	
	2017	2018
Research and development	$143	$180
General and administrative	62	293
Total stock-based compensation expense	$205	$473

6. Stock-Based Compensation (Continued)

As of June 30, 2018, total unrecognized stock-based compensation expense related to unvested options was $3.0 million, which is expected to be recognized over the weighted average period of approximately 2.7 years.

7. Net Loss per Share

Basic and diluted net loss per share is determined by dividing net loss by the weighted average number of shares of common stock outstanding. Because the Company has reported a net loss for the six months ended June 30, 2017 and 2018, diluted net loss per share is the same as basic net loss per share for those periods.

Basic and diluted net loss per share of the Company was calculated as follows (in thousands, except share and per share amounts):

	Six Months Ended June 30,	
	2017	2018
Numerator:		
Net loss	$ (12,428)	$ (16,400)
Denominator:		
Weighted average shares outstanding—basic and diluted	413	12,639
Net loss per share—basic and diluted	$(30,092.01)	$(1,297.57)

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 June 30,	
	2017	2018
Options to purchase shares of common stock	439,032	1,168,938
Redeemable convertible preferred stock (as converted to common stock)	2,822,262	7,474,930
	3,261,294	8,643,868

8. 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.

8. Commitments (Continued)

Rental expense was $0.2 million and $0.3 million for the six months ended June 30, 2017 and 2018, respectively.

Future minimum lease payments for the combined spaces as of June 30, 2018 were as follows (in thousands):

Year Ending December 31,	
2018	$ 260
2019	597
2020	657
2021	710
2022	730
	$2,954

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.

9. 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. As of June 30, 2018, AstraZeneca was the sole A Preferred Stockholder.

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 the six months ended June 30, 2017.

9. Related Party Transactions (Continued)

Lease Commitments

The Company has an operating lease agreement for its office and laboratory space with AstraZeneca. See Note 8.

AstraZeneca Transition Services Agreement

The Company and AstraZeneca entered into a transition services agreement (the "Transition Agreement"), which commenced on May 11, 2015 and expired in November 2015. The Company owed $0.6 million as of December 31, 2016 related to this arrangement, included in due to related party on the consolidated balance sheet, which it paid during the six months ended June 30, 2017.

10. Subsequent Events

The Company evaluated subsequent events through August 17, 2018, the date on which these unaudited consolidated financial statements were issued.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