As submitted confidentially to the Securities and Exchange Commission on January 24, 2018.
This Amendment No. 1 to the draft registration statement has not been publicly filed with the Securities and Exchange Commission
and all information herein remains strictly confidential.

Registration No. 333-
Ordinary Shares, nominal value $0.10 per share

<table>
<thead>
<tr>
<th>Title of Securities being Registered</th>
<th>Proposed Maximum Aggregate Offering Price(1)</th>
<th>Amount of Registration Fee(2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ordinary Shares, nominal value $0.10 per share</td>
<td>$</td>
<td>$</td>
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</tbody>
</table>

(1) Estimated solely for purposes of computing the amount of the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended. Includes the aggregate offering price of additional ordinary shares that underwriters have the option to purchase.

(2) Calculated pursuant to Rule 457(o) under the Securities Act of 1933, as amended, based on an estimate of the proposed maximum aggregate offering price.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

We intend to effect a corporate reorganization prior to the completion of this offering. As part of the corporate reorganization, we intend to change our name from Entasis Therapeutics Limited to EntasisTx Limited and form a new private limited company named Entasis Therapeutics Limited. The shareholders of EntasisTx Limited will exchange their shares for the same number and class of shares in the newly incorporated Entasis Therapeutics Limited, which will ultimately result in EntasisTx Limited becoming a wholly-owned subsidiary of the newly incorporated Entasis Therapeutics Limited. We intend to then re-register Entasis Therapeutics Limited under English law as a public limited company and change our name from Entasis Therapeutics Limited to Entasis Therapeutics plc prior to the completion of this offering. See the section titled “Corporate Reorganization” in the prospectus which forms a part of this registration statement.
This is the initial public offering of ordinary shares of Entasis Therapeutics Limited. We are selling [quantity of shares] of our ordinary shares. Prior to this offering, there has been no public market for our ordinary shares. We anticipate that the initial public offering price will be between $[minimum price] and $[maximum price] per ordinary share. We intend to apply to list our ordinary shares on The Nasdaq Global Market under the symbol “ETTX.”

We have granted the underwriters a 30-day option to purchase up to [additional shares] additional ordinary shares 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 ordinary shares involves risks. See "Risk Factors" on page 14.

<table>
<thead>
<tr>
<th>Per ordinary share</th>
<th>Price to Public</th>
<th>Underwriting Discounts and Commissions</th>
<th>Proceeds to Us, Before Expenses</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>$</td>
<td>$</td>
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</tr>
<tr>
<td>Total</td>
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</table>

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 ordinary shares on or about , 2018.

Credit Suisse
SunTrust Robinson Humphrey

Leerink Partners
Wedbush PacGrow

The date of this prospectus is , 2018.
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 our ordinary shares, and seeking offers to buy our ordinary shares, 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 our ordinary shares. 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 our ordinary shares, 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

Prior to the completion of this offering, we will undertake a corporate reorganization described under the section titled “Corporate Reorganization,” pursuant to which we will change our name to EntasisTx Limited and our shareholders will exchange their shares in EntasisTx Limited for the same class and number of shares in a newly incorporated private limited company, Entasis Therapeutics Limited, which will ultimately result in EntasisTx Limited becoming a wholly owned subsidiary of the newly incorporated Entasis Therapeutics Limited. Entasis Therapeutics Limited will have nominal assets and liabilities and will not have conducted any operations prior to this offering other than acquiring the entire issued share capital of the newly renamed EntasisTx Limited and other actions incidental to such acquisition and its incorporation. Prior to the completion of this offering, we intend to re-register the newly incorporated Entasis Therapeutics Limited as a public limited company and to change its name from Entasis Therapeutics Limited to Entasis Therapeutics plc, convert the entire issued share capital of Entasis Therapeutics plc into a single class of ordinary shares and complete a reverse share split.

Unless otherwise indicated or the context otherwise requires, all references in this prospectus to the terms “Entasis Therapeutics Limited,” “Entasis Therapeutics plc,” “EntasisTx 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 name change of Entasis Therapeutics Limited to EntasisTx Limited, (ii) EntasisTx Limited and its wholly owned U.S. subsidiary, Entasis Therapeutics Inc., prior to the completion of our corporate reorganization, (iii) Entasis Therapeutics Limited and its subsidiaries after the completion of our corporate reorganization and (iv) Entasis Therapeutics plc and its subsidiaries after the re-registration of Entasis Therapeutics Limited as a public limited company and its change of name to Entasis Therapeutics plc, which is expected to occur prior to the completion of this offering. See the section titled “Corporate Reorganization” for more information.

Pursuant to the applicable provisions of the Fixing America's Surface Transportation Act, we are not required to file our consolidated financial statements for the year ended December 31, 2015 because we expect to file our consolidated financial statements for the year ended December 31, 2017 when we first publicly file our registration statement.

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 ordinary shares, 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. Unless the context otherwise requires, we use the terms “Entasis,” “company,” “we,” “us” and “our” in this prospectus to refer to Entasis Therapeutics Limited and, where appropriate, its U.S. subsidiary, Entasis Therapeutics Inc.

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 two lead product candidates, ETX2514 and 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 first product candidate, 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 a Phase 1 clinical trial and, based on a series of discussions with the U.S. Food and Drug Administration, or FDA, we plan to move ETX2514SUL into a single Phase 3 clinical trial in the first quarter of 2019. To optimize the Phase 3 clinical trial, we are conducting additional Phase 1 clinical trials and plan to initiate a Phase 2 clinical trial in the first quarter of 2018. We expect to receive data from these Phase 1 and Phase 2 clinical trials by the end of 2018.

Our second product candidate, ETX0282CPDP, is an oral, fixed-dose combination of ETX0282, a novel oral BLI, with cefpodoxime proxetil, an oral β-lactam antibiotic, that we are developing for the treatment of a variety of serious multi-drug resistant infections caused by Klebsiella pneumoniae, or K. pneumoniae, and Pseudomonas aeruginosa, or P. aeruginosa. We believe there is a significant unmet need for new oral antibiotics that reliably treat patients with multi-drug resistant Gram-negative infections. We believe our preclinical data supports progression to a multi-part Phase 1 clinical trial of ETX0282, which we anticipate initiating in the second quarter of 2018. We expect to receive data from the single-ascending dose escalation part of the trial in the fourth quarter of 2018, and the remainder of the data in the first half of 2019. In addition to our two lead product candidates, we are also developing zoliflodacin, a novel orally administered product candidate that targets bacterial gyrase for the treatment of Neisseria gonorrhoeae, the bacterial pathogen responsible for gonorrhea. We have completed a Phase 2 clinical trial of zoliflodacin and intend to initiate a Phase 3 clinical trial in 2019. The Phase 3 clinical trial is being funded by our non-profit collaborator, the Drugs for Neglected Diseases initiative, or DNDi.

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-b-lactam inhibitors of the penicillin-binding proteins, or NBPs. Penicillin-binding proteins, or PBPs, are clinically validated targets of b-lactam antibiotics, such as penicillins and carbapenems. Due to their differentiated chemical structure, our NBPs are not subject to inactivation by b-lactamases, unlike b-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:

<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Upcoming Milestones</th>
<th>Commercial Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETX2514SUL IV</td>
<td>Multi-drug resistant Acinetobacter infections</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initiate Phase 3 trial in 1Q 2019(1); data expected in 2020</td>
<td>Worldwide</td>
</tr>
<tr>
<td></td>
<td>Carbapenem-resistant infections (Pseudomonas, CRE and others)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initiate Phase 2 trial in 1Q 2018; data expected by the end of 2018(2)</td>
<td>Worldwide</td>
</tr>
<tr>
<td>ETX0382CPDP Oral</td>
<td>Complicated UTIs (Enterobacteriaceae including ESBL-producing and CRE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initiate Phase 1 trial in 5Q 2018; SAD data expected in 4Q 2018 and remainder of the data in 1H 2019</td>
<td>Worldwide</td>
</tr>
<tr>
<td>Zoilitodacin Oral</td>
<td>Uncomplicated gonorrhea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initiate Phase 3 trial in 2019</td>
<td>All developed countries(3)</td>
</tr>
<tr>
<td>NBP Program IV</td>
<td>Gram-negative infections (initially multi-drug resistant Pseudomonas)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Select initial clinical candidates in 2019</td>
<td>Worldwide</td>
</tr>
</tbody>
</table>

(1) We have completed a Phase 1 clinical trial and, based on a series of discussions with the FDA, we plan to move ETX2514SUL IV into a single Phase 3 clinical trial in the first quarter of 2019.

(2) Safety and pharmacokinetic data from the Phase 2 trial will be used to support the NDA package for ETX2514SUL IV.

(3) 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 in which ETX2514 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 initiated two additional Phase 1 clinical trials to evaluate drug penetration into the lung and to assess pharmacokinetics in renally impaired patients. In parallel with these additional Phase 1 clinical trials, we have also chosen to conduct a Phase 2 clinical trial in patients with complicated UTIs 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 Primaxin™ in our clinical trials to provide broad coverage for these other pathogens. Primaxin is an FDA-approved fixed-dose combination of imipenem, a carbapenem antibiotic, and cilastatin, a drug that prevents degradation of imipenem. Throughout our clinical trials, we plan to collect data on the activity of ETX2514SUL in combination with Primaxin against a range of Gram-negative pathogens in addition to Acinetobacter. Based on the results of our preclinical studies, 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.

**ETX0282CPDP**

We are developing ETX0282CPDP, an oral fixed-dose combination of ETX0282 with cepodoxime proxetil, or cepodoxime, 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 b-lactamases, which are the primary mechanisms of resistance associated with multi-drug resistant *Enterobacteriaceae* infections. Cepodoxime was once used to treat UTIs, among other indications, but its clinical utility is currently limited by b-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 3.5 million to 4.5 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 b-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. Based on our preclinical data, we anticipate initiating a multi-part Phase 1 clinical trial of ETX0282 in Australia in the second quarter of 2018. We expect to receive data from the single-ascending dose escalation part of the trial in the fourth quarter of 2018 and the remainder of the data in the first half of 2019.

**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, 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-labeled 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 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.

**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 two lead product candidates, ETX2514SUL and ETX0282CPDP, 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 initiate a multi-part Phase 1 clinical trial of ETX0282 in the second quarter of 2018. We expect to receive data from the single-ascending dose escalation part of the trial in the fourth quarter of 2018 and the remainder of the data in the first half of 2019. We also plan to explore additional indications with these product candidates. For example, based on the results of our preclinical studies, 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 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. We plan to initiate a Phase 3 clinical trial in 2019, which will be fully funded by DNDi. 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.

- **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 nonprofit organizations, government agencies and other third parties, including DNDi, the U.S. National Institute of Allergy and Infectious Diseases, or NIAID, 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 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, 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 ordinary shares. 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.

• The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation.
We are an "emerging growth company" and as a result of the reduced disclosure and governance requirements applicable to emerging
growth companies, our ordinary shares may be less attractive to investors.

Because we expect to be a passive foreign investment company following this offering, there could be adverse U.S. federal income tax
consequences to U.S. Holders.

Corporate Information

Entasis Therapeutics Limited was incorporated under the laws of England and Wales on March 6, 2015. We changed our name to EntasisTx Limited on
, 2018. Our registered office address, as listed with the Companies House in the United Kingdom, is 3rd floor, 1 Ashley Road, Altrincham,
Cheshire WA14 2DT, United Kingdom and our telephone number is +44 (0)161 942 4700. 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 our ordinary shares.

Upon completion of this offering, we will have two wholly owned subsidiaries, EntasisTx Limited, which was incorporated under the laws of England
and Wales as Entasis Therapeutics Limited on March 6, 2015 and which changed its name to EntasisTx Limited in connection with this offering, and
Entasis Therapeutics Inc., which was incorporated under the laws of the State of Delaware on March 11, 2015.

Corporate Reorganization

The newly formed Entasis Therapeutics Limited was incorporated as a private limited company pursuant to the laws of England and Wales on
, 2018. Pursuant to the terms of a corporate reorganization that will be completed prior to the closing of this offering, the entire issued share
capital of the newly renamed EntasisTx Limited will ultimately be exchanged for the same number and classes of newly issued shares of the newly formed
Entasis Therapeutics Limited and, as a result, EntasisTx Limited will become a wholly owned subsidiary of the newly formed Entasis Therapeutics
Limited. Prior to the consummation of this offering, the newly formed Entasis Therapeutics Limited will re-register as a public limited company and
change its name to Entasis Therapeutics plc. 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 shareholder 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 ordinary shares that are 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

**Ordinary shares offered by us**  
Ordinary shares

**Ordinary shares to be outstanding immediately after this offering**  
Ordinary shares

**Option to purchase additional ordinary shares**  
We have granted the underwriters an option for a period of 30 days from the date of this prospectus to purchase up to additional ordinary shares.

**Use of proceeds**  
We estimate that the net proceeds to us from this offering will be approximately $ million, assuming an initial public offering price of $ per ordinary 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, including the completion of an additional Phase 1 and Phase 2 clinical trial;
- to fund the advancement of ETX0282 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 ordinary shares.

**Proposed Nasdaq Global Market symbol**  
ETTX

The number of ordinary shares that will be outstanding after this offering is based on ordinary shares outstanding as of December 31, 2017, after giving effect to the automatic conversion of all of our outstanding preference shares into ordinary shares upon the closing of this offering, and excludes:

- ordinary shares issuable upon the exercise of share options outstanding under our amended and restated stock incentive plan, or our 2015 Plan, as of December 31, 2017, at a weighted average exercise price of $ per ordinary share;
ordinary shares reserved and available for future issuance under our 2015 Plan as of December 31, 2017; and

ordinary shares 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 ordinary shares reserved for issuance under our 2018 Plan.

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

- the consummation of the transactions described under the section titled “Corporate Reorganization” prior to the closing of this offering;

- a reverse share split of our ordinary shares expected to be completed prior to the completion of this offering;

- the automatic conversion of all of our outstanding preference shares into an aggregate of ordinary shares upon the closing of this offering;

- no exercise of the outstanding options described above; and

- no exercise of the underwriters’ option to purchase additional ordinary shares.
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 and our consolidated balance sheet data as of December 31, 2017 from our audited consolidated financial statements appearing elsewhere in this prospectus. 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.

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>(in thousands, except share and per-share data)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Consolidated Statement of Operations Data:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operating expenses:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>$15,778</td>
<td>$</td>
</tr>
<tr>
<td>General and administrative</td>
<td>3,326</td>
<td></td>
</tr>
<tr>
<td><strong>Total operating expenses</strong></td>
<td></td>
<td>19,104</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(19,104)</td>
<td></td>
</tr>
<tr>
<td>Other income:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interest income</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td><strong>Total other income</strong></td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td>$ (19,095)</td>
<td>$</td>
</tr>
<tr>
<td>Net loss per share—basic and diluted(1)</td>
<td>$ (190,950.00)</td>
<td>$</td>
</tr>
<tr>
<td>Weighted-average ordinary shares outstanding—basic and diluted(1)</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Pro forma net loss per share(1)</td>
<td>$</td>
<td></td>
</tr>
<tr>
<td>Pro forma weighted-average ordinary shares outstanding—basic and diluted(1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(1\) See Note 2 to our consolidated financial statements appearing elsewhere in this prospectus for further details on the calculation of basic and diluted net loss per ordinary share.
The following table presents our consolidated summary balance sheet data:

- on an actual basis as of December 31, 2017;
- on a pro forma basis to give effect to the automatic conversion of all then outstanding preference shares into an aggregate of ordinary shares upon the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to our sale of ordinary shares in this offering at an assumed initial public offering price of $ per ordinary 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.

<table>
<thead>
<tr>
<th>Consolidated Balance Sheet Data:</th>
<th>As of December 31, 2017</th>
<th>Actual</th>
<th>Pro forma (in thousands)</th>
<th>Pro forma as adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash and cash equivalents</td>
<td></td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>Working capital</td>
<td></td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>Total assets</td>
<td></td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>Total liabilities</td>
<td></td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>Redeemable convertible preference shares</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total shareholders’ equity (deficit)</td>
<td></td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
</tbody>
</table>

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 $ per ordinary 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 shareholders’ equity by $ million, assuming that the number of ordinary 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 ordinary shares we are offering. Each increase or decrease of 1.0 million ordinary shares in the number of ordinary shares offered by us would increase or decrease each of cash and cash equivalents, working capital, total assets and total shareholders’ equity by $ 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 ordinary shares involves a high degree of risk. Before you invest in our ordinary shares, 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 ordinary shares 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 $ million for the year ended December 31, 2017 and $19.1 million for the year ended December 31, 2016. As of December 31, 2017, we had an accumulated deficit of $ million. We have funded our operations to date primarily with proceeds from the sale of our preference shares. 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 non-profit awards from the Drugs for Neglected Diseases initiative, or DNDi.

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
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 ordinary shares 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 ordinary shares could also cause you to lose all or part of your investment.

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

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

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

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

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

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements until . 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 shareholders, including purchasers of ordinary shares 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 an ordinary shareholder. 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, ETX0282CPDP and zoliflodacin 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, ETX0282CPDP, zoliflodacin 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 ordinary shares.

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 evaluating drug penetration into the lung, the ongoing Phase 1 clinical trial assessing pharmacokinetics in renally impaired patients and the planned 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, ETX0282CPDP, zoliflodacin 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, ETX0282CPDP, zoliflodacin 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, ETX0282CPDP, zoliflodacin 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, ETX0282CPDP, zoliflodacin 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, ETX0282CPDP, zoliflodacin 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, ETX0282CPDP, zoliflodacin 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, ETX0282CPDP and zoliflodacin, 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, ETX0282CPDP or zoliflodacin.

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, ETX0282CPDP, zoliflodacin 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 ordinary shares 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. 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, ETX0282CPDP and zoliflodacin, 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 ordinary shares 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 two lead product candidates, ETX2514 and ETX0282, inhibit one of the most prevalent forms of bacterial resistance, b-lactamase enzymes, so-named because of their ability to inactivate b-lactam antibiotics, one of the most commonly used classes of antibiotics. By blocking this resistance mechanism, these product candidates, when administered in combination with b-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 lead 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 lead product candidates, we may not be able to complete their clinical development on our current timeline or at all.

Even if our lead 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 lead product candidates or that safety, efficacy, manufacturing or supply issues could arise with these existing drugs.

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, ETX0282CPDP, zoliflodacin 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 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 collaboration with 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 DNDi to adequately perform its obligations and responsibilities in the conduct of the planned Phase 3 clinical trial of zoliflodacin could harm our business because we may not obtain regulatory approval for zoliflodacin in a timely manner, or at all.

We have 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, DNDi has agreed to fund all of the Phase 3 development costs of zoliflodacin, including the manufacture and supply of the product candidate containing zoliflodacin, and will take the lead in Phase 3 clinical development activities. While we expect to provide operational and logistical support for the clinical trial, we have limited control of their activities. We cannot control whether or not DNDi will devote sufficient time and resources to the clinical trial. If DNDi does not successfully carry out its obligations and responsibilities or meet expected deadlines or if the quality or accuracy of the clinical data it obtains is compromised due to the failure to adhere to clinical protocols, regulatory requirements or for other reasons, the Phase 3 clinical trial may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, zoliflodacin. As a result, our results of operations and the commercial prospects for zoliflodacin would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Although DNDi is responsible for conducting the planned Phase 3 clinical trial of zoliflodacin, 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 DNDi 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 shareholders. 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
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, ETX0282CPDP, and zoliflodacin 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, ETX0282CPDP, zoliflodacin 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, ETX0282CPDP, zoliflodacin 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 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 plazomicin. 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
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 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 addressing gonorrhea.

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.
The United Kingdom’s vote in favor of withdrawing from the European Union, or EU, may have a negative effect on global economic conditions, financial markets and our business, which could reduce the market price of our ordinary shares and make it more difficult to do business in Europe.

In June 2016, a majority of the eligible members of the electorate in the United Kingdom voted to withdraw from the EU in a national referendum, commonly referred to as “Brexit.” The withdrawal of the United Kingdom from the EU will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to Article 50 of the Treaty on European Union, unless the European Council, in agreement with the United Kingdom, unanimously decides to extend this period. On March 29, 2017, the United Kingdom formally delivered the notice of withdrawal to the EU. It appears likely that this withdrawal will involve a process of lengthy negotiations between the United Kingdom and EU Member States to determine the future terms of the United Kingdom’s relationship with the EU.

These developments, or the perception that any of them could occur, have had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the U.K. financial and banking markets, as well as on the regulatory process in Europe. As a result of this uncertainty, global financial markets could experience significant volatility, which could adversely affect the market price of our ordinary shares. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which EU rules and regulations to replace or replicate in the event of a withdrawal, including financial laws and regulations, tax and free trade agreements, intellectual property rights, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, could decrease foreign direct investment in the United Kingdom, increase costs, depress economic activity and restrict our access to capital. If the United Kingdom and the EU are unable to negotiate acceptable withdrawal terms or if other EU Member States pursue withdrawal, barrier-free access between the United Kingdom and other EU Member States or among the European Economic Area overall could be diminished or eliminated.

We may also face new regulatory costs and challenges that could have an adverse effect on our operations. Depending on the terms of Brexit, the United Kingdom could lose the benefits of global trade agreements negotiated by the EU on behalf of its members, which may result in increased trade barriers that could make our doing business in Europe more difficult. In addition, currency exchange rates in the pound sterling and the euro with respect to each other and the U.S. dollar have already been adversely affected by Brexit. Furthermore, at present, there are no indications of the effect Brexit will have on the pathway to obtaining marketing approval for any of our product candidates in the United Kingdom, or what, if any, role the EMA may have in the approval process.

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 closing of this offering, each of them may currently terminate their employment with us at any time.
and will continue to be able to do so after the closing 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 December 1, 2017, we had 30 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.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a significant disruption of our product development programs and our ability to operate our business effectively.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. 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. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or
proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

If we engage in future acquisitions or strategic collaborations, this may increase our capital requirements, dilute our shareholders, 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 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 ordinary shares. 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, ETX0282CPDP, zoliflodacin 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 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 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 and civil monetary penalty 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 new 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 healthcare benefit program, willfully obstructing a criminal investigation of a healthcare 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 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; 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, ETX0282CPDP, zoliflodacin 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 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. The Trump administration has also announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for the CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments has been introduced in the Senate, but the future of that bill is uncertain. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, each chamber of
Congress has put forth multiple bills this year designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, 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.

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 Ordinary Shares and Our Status as a Public Company

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

This offering constitutes the initial public offering of our ordinary shares, and no public market has previously existed for our ordinary shares. We intend to apply to list our ordinary shares on The Nasdaq Global Market. Any delay in the commencement of trading of our ordinary shares on The Nasdaq Global Market would impair the liquidity of the market for the ordinary shares and make it more difficult for holders to sell the ordinary shares. If the ordinary shares are listed and quoted on The Nasdaq Global Market, there can be no assurance that an active trading market for the ordinary 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 ordinary shares will trade at a price equal to or greater than the public offering price.

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

The trading price of our ordinary shares 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 ordinary 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 ordinary shares on The Nasdaq Global Market;
• sales of our ordinary shares by us, our executive officers and directors or our shareholders 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 ordinary shares to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from selling their ordinary shares at or above the price paid for the shares and may otherwise negatively affect the liquidity of our ordinary shares. 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 ordinary shares.

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

The trading market for our ordinary shares 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 ordinary shares after the completion of this offering, and such lack of research coverage may adversely affect the market price of our ordinary shares. 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 ordinary shares to decline.

**If you purchase ordinary shares in this offering, you will suffer immediate dilution of your investment.**

The initial public offering price of our ordinary shares is substantially higher than the pro forma as adjusted net tangible book value per ordinary share. Therefore, if you purchase ordinary shares 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 $ 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 $ per share, representing the difference between our pro forma as adjusted net tangible book value per share after this offering and the initial public offering price per share. After this offering, we will also have outstanding options to purchase ordinary shares with exercise prices lower than the initial public offering price per share. 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 ordinary shares to drop significantly, even if our business is doing well.

Sales of a substantial number of our ordinary shares in the public market could occur at any time. If our shareholders sell, or the market perceives that our shareholders intend to sell, substantial amounts of our ordinary shares in the public market following this offering, the market price of our ordinary shares could decline significantly.

Upon completion of this offering, we will have outstanding ordinary shares, based on the number of ordinary shares outstanding as of December 31, 2017 and after giving effect to the automatic conversion of all outstanding preference shares into ordinary shares upon the closing of this offering. Of these shares, the shares sold in this offering will be freely tradable, and additional ordinary shares 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 shareholders and the underwriters. The representatives of the underwriters may release these shareholders from their lock-up agreements with the underwriters at any time and without notice, 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 ordinary shares 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.

Additionally, after this offering, the holders of an aggregate of of our ordinary shares, 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 shareholders. 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 ordinary shares could decline.

The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation.

We are incorporated under English law. The rights of holders of ordinary shares are governed by English law, including the provisions of the U.K. Companies Act 2006, or the Companies Act, and by our Articles of Association. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations. See the section titled “Description of Share Capital and Articles of Association—Differences in Corporate Law” in this prospectus for a description of the principal differences between the provisions of the Companies Act applicable to us and, for example, the Delaware General Corporation Law relating to shareholders’ rights and protections.

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

Upon completion of this offering, our executive officers, directors and current beneficial owners of 5% or more of our ordinary shares and their respective affiliates will, in the aggregate, beneficially own approximately % of our outstanding ordinary shares, based on the number of ordinary shares outstanding as of December 31, 2017 and after giving effect to the automatic conversion of all outstanding preference shares into ordinary shares upon the closing of this offering. As a result, these persons, acting together, would be able to significantly influence all matters requiring shareholder 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 ordinary shares 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 shareholders 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 shareholders.

Anti-takeover provisions in our articles of association could make an acquisition of us, which may be beneficial to our shareholders, more difficult and may prevent attempts by our shareholders to replace or remove our current management and limit the market price of our ordinary shares.

Provisions in our articles of association that will become effective upon the closing of this offering may discourage, delay or prevent a merger, acquisition or other change in control of us that shareholders may consider favorable, including transactions in which you might otherwise receive a premium for your ordinary shares. These provisions also could limit the price that investors might be willing to pay in the future for our ordinary shares, thereby depressing the market price of our ordinary shares.

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shares. 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 shareholders to replace or remove our current management by making it more difficult for shareholders to replace members of our board of directors. For example, our articles of association that will be in effect upon the completion of this offering establish a classified board of directors such that not all members of our board are elected at one time. In addition, the Companies Act requires that shareholder resolutions are passed at a general meeting of the shareholders; as such, shareholder resolutions cannot be passed by unanimous written consent. See the section titled “Description of Share Capital and Articles of Association—Post-IPO Articles of Association.”

Any provision of our articles of association or English law that has the effect of delaying or deterring a change of control could limit the opportunity for our shareholders to receive a premium for their ordinary shares, and could also affect the price that some investors are willing to pay for our ordinary shares.

We are an "emerging growth company" and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our ordinary shares 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 shareholder approval of any golden parachute payments not previously approved.

We cannot predict if investors will find our ordinary shares less attractive because we will rely on these exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and our share price may 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 ordinary shares 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 ordinary shares 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 ordinary shares. 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 ordinary shares 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 ordinary shares 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 ordinary shares to provide dividend income. Under current English law, a company's accumulated realized profits must exceed its accumulated realized losses (on a non-consolidated basis) before dividends can be paid. Therefore, we must have distributable profits before issuing a dividend. Additionally, 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 ordinary shares 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 shareholders until the applicable milestone payment has been paid in full or otherwise waived. We have never declared or paid a dividend on our ordinary shares 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 ordinary shares will be your sole source of gains for the foreseeable future. Investors seeking cash dividends should not purchase our ordinary shares in this offering.

Because we expect to be a passive foreign investment company following this offering, there could be adverse U.S. federal income tax consequences to U.S. Holders.

Under the Internal Revenue Code of 1986, as amended, or the Code, we will be a passive foreign investment company, or PFIC, for any taxable year in which (1) 75% or more of our gross income consists of passive income or (2) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, passive income. For purposes of these tests, passive income includes dividends, interest, gains from the sale or exchange of investment property and certain rents and royalties. In addition, for purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as if it held its proportionate share of the assets and received directly its proportionate share of the income of such other corporation. If we are a PFIC for any taxable year during which a U.S. Holder (as defined below under "Material Income Tax Considerations—Material U.S. Federal Income Tax Considerations for U.S. Holders") holds our shares, the U.S. Holder may be subject to adverse tax consequences regardless of whether we continue to qualify as a PFIC, including ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements.

We believe that we were a PFIC for the calendar year ended December 31, 2016. Based on our estimates of expected gross assets and income, we believe that we will be classified as a PFIC for the calendar year ending December 31, 2017. We cannot provide any assurances regarding our PFIC status for any past, current or future taxable years. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis and the applicable law is subject to varying interpretation. In particular, the characterization of our assets as active or passive may depend in part on our current and intended future business plans, which are subject to change. In addition, for our current and future taxable years, the total value of our assets for PFIC testing purposes may be determined in part by reference to the market price of our ordinary shares from time to time, which may fluctuate considerably. Under the income test, our status as a PFIC depends on the composition of our income which will depend on the transactions we enter into in the future and our corporate structure. The composition of our income and assets is also affected by how, and how quickly, we spend the cash we raise in any offering, including this offering.

For further discussion of the PFIC rules and the adverse U.S. federal income tax consequences in the event we are classified as a PFIC, see the section titled "Material Income Tax Considerations—Material U.S. Federal Income Considerations for U.S. Holders."

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 $ [ ] million, $ [ ] million and $ [ ] 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
The deductibility of federal net operating losses is limited. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. The NOLs in the United Kingdom can be carried forward indefinitely. 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, 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 shareholders over a three-year period, the corporation’s ability to use its pre-change net operating loss carryforwards, or 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 will 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 related to the Organisation for Economic Co-Operation and Development’s, or OECD, Base Erosion and Profit Shifting, or BEPS, Project, the European Commission’s state aid investigations 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 that significantly revises the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, 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 ordinary shares is also uncertain and could be adverse. Other legislative changes could also affect the taxation of holders of our ordinary shares. 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 shareholders 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 ordinary shares.
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. 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 ordinary shares are 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.
Shareholder protections found in provisions under the U.K. City Code on Takeovers and Mergers, or the Takeover Code, will apply if our place of management and control remains in the United Kingdom.

We believe that as of the date of this prospectus our place of central management and control is in the United Kingdom for the purposes of the jurisdictional criteria of the Takeover Code. Accordingly, we believe that we are currently subject to the Takeover Code and, as a result, our shareholders are currently entitled to the benefit of certain takeover offer protections provided under the Takeover Code, including the rules regarding mandatory takeover bids.

The Takeover Code provides a framework within which takeovers of companies are regulated and conducted. The Takeover Panel may, at any relevant time, review our place of central management and control based on the jurisdictional criteria of the Takeover Code, and their assessment as to jurisdiction may or may not change. Absent a relevant event occurring under the Takeover Code, it is unlikely that the Takeover Panel would re-assess jurisdiction in the interim. It is feasible that, in the future, due to the board's composition, location of board meetings, changes in the Takeover Panel's interpretation of the Takeover Code or other events, the Takeover Panel's assessment of its jurisdiction regarding and applicability of the Takeover Code to the Company may change.

The following is a brief summary of some of the most important rules of the Takeover Code:

• When either (i) a person, together with persons acting in concert with him, acquires, whether by a series of transactions over a period of time or not, an interest in shares which (when taken together with shares in which persons acting in concert with him are interested) carry 30% or more of the voting rights of a company (which percentage is treated by the Takeover Code as the level at which effective control is obtained); or (ii) any person who, together with persons acting in concert with him, is interested in shares which in the aggregate carry not less than 30% of the voting rights of a company but does not hold shares carrying more than 50% of such voting rights and such person, or any person acting in concert with him, acquires an interest in any other shares which increases the percentage of shares carrying voting rights in which he is interested, such person must make a cash offer to all other shareholders at not less than the highest price paid by the person required to make an offer or any person acting in concert with him during the 12 months before the offer was announced.

• If an offer has been made for a company and interests in shares carrying 10% or more of the voting rights of a class have been acquired by the offeror (i.e., a bidder) in the offer period and the previous 12 months, the offer must include a cash alternative for all shareholders of that class at the highest price paid by the offeror in that period. Further, if an offeror acquires for cash any interest in shares during the offer period, a cash alternative must be made available at a price at least equal to the price paid for such shares.

• If, after making an offer for a company, the offeror acquires an interest in shares in an offeree company (i.e., a target) at a price higher than the value of the offer, the offer must be increased accordingly.

• An offeree company must appoint a competent independent adviser whose advice on the financial terms of the offer must be made known to all the shareholders, together with the opinion of the board of directors of the offeree company.

• Favorable deals for selected shareholders are banned.

• All shareholders must be given the same information.

• Those issuing takeover circulars must include statements taking responsibility for the contents thereof.
Profit forecasts, quantified financial benefits statements and asset valuations must be made to specified standards and must be reported on by professional advisers.

Misleading, inaccurate or unsubstantiated statements made in documents or to the media must be publicly corrected immediately.

Actions during the course of an offer by the offeree company, which might frustrate the offer are generally prohibited unless shareholders approve these plans.

Stringent requirements are laid down for the disclosure of dealings in relevant securities during an offer.

Employees of both the offeror and the offeree company and the trustees of the offeree company's pension scheme must be informed about an offer. In addition, the offeree company's employee representatives and pension scheme trustees have the right to have a separate opinion on the effects of the offer on employment appended to the offeree board of directors' circular or published on a website.

Transfers of our ordinary shares, other than one effected by means of the transfer of book-entry interests in the Depository Trust Company, or DTC, may be subject to U.K. stamp duty.

Upon completion of this offering, certain of our outstanding shares will be represented by book-entry interests in DTC. Transfers of our ordinary shares within DTC should not be subject to stamp duty or stamp duty reserve tax, or SDRT, provided no instrument of transfer is entered into and no election that applies to our ordinary shares is made or has been made by DTC or Cede, its nominee, under Section 97A of the U.K. Finance Act 1986, or the Finance Act. In this regard, we are not aware of any election by DTC under Section 97A of the Finance Act that would affect our shares issued to Cede. If such an election is or has been made, transfers of our ordinary shares within DTC generally will be subject to SDRT at the rate of 0.5% of the amount or value of the consideration. Transfers of our ordinary shares held in certificated form generally will be subject to stamp duty at the rate of 0.5% of the consideration given (rounded up to the nearest £5). SDRT will also be chargeable on an agreement to transfer such shares, although such liability would be discharged if stamp duty is duly paid on the instrument of transfer implementing such agreement within a period of six years from the agreement. Subsequent transfer of our ordinary shares to an issuer of depository receipts or into a clearance system (including DTC) may be subject to SDRT at a rate of 1.5% of the consideration given or received or, in certain cases, the value of our ordinary shares transferred. The purchaser or transferee of the ordinary shares generally will be responsible for paying any stamp duty or SDRT payable.

Claims of U.S. civil liabilities may not be enforceable against certain directors or us.

We are incorporated and have our registered office in, and are currently existing under the laws of, England and Wales. In addition, while our officers all currently reside in and most of our tangible assets are located inside the United States, certain of our directors reside and some of our assets are held outside of the United States. As a result, it may not be possible to serve process within the United States on certain directors or us or to enforce judgments obtained in U.S. courts against such directors or us based on civil liability provisions of the securities laws of the United States. As a result, it may not be possible for investors to effect service of process within the United States upon such persons or to enforce judgments obtained in U.S. courts against them or us, including judgments predicated upon the civil liability provisions of the U.S. federal securities laws.

The United States and the United Kingdom do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters. Consequently, a final judgment for payment given by a court in the United States, whether or
not predicated solely upon U.S. securities laws, would not automatically be recognized or enforceable in the United Kingdom. In addition, uncertainty exists as to whether U.K. courts would entertain original actions brought in the United Kingdom against us or our directors or senior management predicated upon the securities laws of the United States or any state in the United States. Any final and conclusive monetary judgment for a definite sum obtained against us in U.S. courts would be treated by the courts of the United Kingdom as a cause of action in itself and sued upon as a debt at common law so that no retrial of the issues would be necessary, provided that certain requirements are met. Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the U.S. securities laws, including whether the award of monetary damages under such laws would constitute a penalty, is an issue for the court making such decision. If an English court gives judgment for the sum payable under a U.S. judgment, the English judgment will be enforceable by methods generally available for this purpose. These methods generally permit the English court discretion to prescribe the manner of enforcement.

As a result, U.S. investors may not be able to enforce against us or certain of our directors any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.
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;
• our estimates regarding the market opportunities for our product candidates;
• our intellectual property position and the duration of our patent rights;
• our anticipated PFIC status;
• 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 ordinary shares in this offering will be approximately $ million, or approximately $ million if the underwriters exercise their option to purchase additional ordinary shares in full, assuming an initial public offering price of $ per ordinary 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 $ per ordinary 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 $ million, assuming that the number of ordinary 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 ordinary shares we are offering. Each increase or decrease of 1.0 million in the number of ordinary shares we are offering at the assumed initial public offering price would increase or decrease the net proceeds to us from this offering by $ million, assuming no change in the assumed initial public offering price per ordinary share and after deducting estimated underwriting discounts and commissions.

As of December 31, 2017, we had cash and cash equivalents of $ 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 $ million to fund the advancement of ETX2514SUL through a Phase 3 clinical trial, including the completion of an additional Phase 1 clinical trial and a Phase 2 clinical trial;
• approximately $ million to fund the advancement of ETX0282 through a multi-part Phase 1 clinical trial;
• approximately $ million 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 other general corporate purposes.

We may also use a portion of the remaining net proceeds 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 ETX0282 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, these 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 for at least the next months. 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. See “Risk Factors—Risks Related to this Offering, Ownership of Our Ordinary Shares and Our Status as a Public Company—Because we do not anticipate paying any cash dividends on our ordinary shares 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.”

Under English law, we may only pay dividends if we have sufficient distributable reserves (on a non-consolidated basis), which are our accumulated realized profits that have not been previously distributed or capitalized less our accumulated realized losses, so far as such losses have not been previously written off in a reduction or reorganization of capital. Additionally, 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 shareholders 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 intend to effect a corporate reorganization prior to the completion of this offering. As part of the corporate reorganization, we intend to change our name from Entasis Therapeutics Limited to EntasisTx Limited and form a new private limited company named Entasis Therapeutics Limited. The newly formed Entasis Therapeutics Limited will be incorporated in England and Wales on [date], 2018 with nominal assets and liabilities for the purpose of consummating the corporate reorganization described herein. In connection with the corporate reorganization, the old Entasis Therapeutics Limited will change its name to EntasisTx Limited and its shareholders will exchange their shares for the same number and class of shares in Entasis Therapeutics Limited. As a result, EntasisTx Limited will become a wholly owned subsidiary of Entasis Therapeutics Limited. Subsequently, we intend to re-register the newly formed Entasis Therapeutics Limited as a public limited company and change its name to Entasis Therapeutics plc, convert the entire issued share capital of Entasis Therapeutics plc into a single class of ordinary shares and complete a [number-to-number] reverse share split. Therefore, investors in this offering will only acquire, and this prospectus only describes the offering of, ordinary shares of Entasis Therapeutics plc. We refer to the reorganization described in this "Corporate Reorganization" section as our "corporate reorganization." The corporate reorganization will take place in several steps, all of which will be completed prior to the completion of this offering.

Change of Name of Entasis Therapeutics Limited to EntasisTx Limited; Incorporation of New Entity

In order to retain the name Entasis Therapeutics, we first need to change the name of Entasis Therapeutics Limited to EntasisTx Limited as two companies are not permitted to have the same name under English law. Such change of name will require the passing of a special resolution by the shareholders of Entasis Therapeutics Limited. The newly formed Entasis Therapeutics Limited was incorporated pursuant to the laws of England and Wales on [date], 2018. All subsequent references to Entasis Therapeutics Limited in this "Corporate Reorganization" section refer to this newly formed limited company.

Exchange of EntasisTx Limited Shares for Entasis Therapeutics Limited Shares

Prior to this offering, the share capital of the newly renamed EntasisTx Limited was divided into ordinary shares, A preference shares, B preference shares and B-1 preference shares. Prior to the effectiveness of the registration statement of which this prospectus forms a part, the shareholders of the newly renamed EntasisTx Limited will exchange each of these classes of shares of EntasisTx Limited for the same number and class of shares of the newly incorporated Entasis Therapeutics Limited on a one-to-one basis. As a result, the newly formed Entasis Therapeutics Limited will become the sole shareholder of the newly renamed EntasisTx Limited and the shareholders of EntasisTx Limited will solely hold shares in the newly formed Entasis Therapeutics Limited.

The deferred shares in the capital of EntasisTx Limited will be re-purchased prior to this reorganization, funded out of distributable reserves from a reduction of capital by EntasisTx Limited.

Re-Registration of Entasis Therapeutics Limited as a Public Limited Company and Change of Name to Entasis Therapeutics plc

In order to re-register as a public limited company, a private limited company must comply with certain statutory requirements under English law, including the requirement that the sum of its net assets are not less than the sum of its paid up share capital and undistributable reserves. The newly re-named EntasisTx Limited has accumulated losses during previous financial years and will not satisfy this requirement. As a result, it is necessary to incorporate the newly formed Entasis Therapeutics Limited to become the holding company, as this entity will not have accumulated losses and will be re-registrable as a public liability company. Following the newly renamed EntasisTx Limited becoming a
wholly owned subsidiary of the newly incorporated Entasis Therapeutics Limited, prior to the completion of this offering, the newly formed Entasis Therapeutics Limited will re-register as a public limited company and, in compliance with the statutory requirements under English law, change its name to Entasis Therapeutics plc.

Conversion of Entasis Therapeutics plc Shares into Ordinary Shares

In order to have one class of stock upon the completion of this offering, all A preference shares, B preference shares, B-1 preference shares and ordinary shares of Entasis Therapeutics plc will be converted into ordinary shares of Entasis Therapeutics plc on a one-to-one basis prior to the completion of this offering. Therefore, upon completion of this offering, the current shareholders of EntasisTx Limited will hold an aggregate of ordinary shares of Entasis Therapeutics plc.

Reverse Share Split

In connection with our corporate reorganization, we intend to effect a reverse share split of our ordinary shares.
CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of December 31, 2017:

• on an actual basis;

• on a pro forma basis giving effect to the automatic conversion of all of our outstanding preference shares into an aggregate of ordinary shares upon the closing of this offering;

• on a pro forma as adjusted basis to give further effect to our sale of ordinary shares in this offering at an assumed initial public offering price of $ per ordinary 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 December 31, 2017

<table>
<thead>
<tr>
<th></th>
<th>Actual</th>
<th>Pro forma</th>
<th>Pro forma as adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(in thousands, except share and per-share data)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cash and cash equivalents</strong></td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>A redeemable convertible preference shares, nominal value $1.00 per share; 33,499,900 shares issued and outstanding, actual; no shares issued and outstanding, pro forma and pro forma as adjusted</td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>B redeemable convertible preference shares, nominal value $1.00 per share; 25,000,000 shares issued and outstanding, actual; no shares issued and outstanding, pro forma and pro forma as adjusted</td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>B-1 redeemable convertible preference shares, nominal value $0.59 per share; 96,440,678 shares issued and outstanding, actual; no shares issued and outstanding, pro forma and pro forma as adjusted</td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td><strong>Shareholders' equity (deficit):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ordinary shares, nominal value $0.20 per share; 33,499,900 ordinary shares issued and outstanding, actual; 25,000,000 ordinary shares issued and outstanding, pro forma and pro forma as adjusted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional paid-in capital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accumulated deficit</td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td><strong>Total shareholders' equity (deficit)</strong></td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>Total capitalization</td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
</tbody>
</table>

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 $ per ordinary 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, additional paid-in capital, total shareholders' equity and total capitalization by $ million, assuming that the number of ordinary

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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 or decrease of 1.0 million in the number of ordinary 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 shareholders’ equity and total capitalization by $\text{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 ordinary shares outstanding in the table above does not include:

- ordinary shares issuable upon the exercise of share options outstanding under our 2015 Plan as of December 31, 2017, at a weighted average exercise price of $\text{per ordinary share};
- ordinary shares reserved and available for future issuance under our 2015 Plan as of December 31, 2017; and
- ordinary shares 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 ordinary shares reserved for issuance under our 2018 Plan.
DILUTION

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

As of December 31, 2017, we had a net tangible book deficit of $( ) million, or $( ) per ordinary share. On a pro forma basis, after giving effect to the automatic conversion of all of our outstanding preference shares as of December 31, 2017 into an aggregate of ordinary shares upon the closing of this offering, our pro forma net tangible book value would have been $ million, or $ per ordinary share.

After giving effect to the issuance and sale of ordinary shares in this offering at an assumed initial public offering price of $ per ordinary 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 December 31, 2017 would have been $ million, or $ per ordinary share. This represents an immediate increase in the pro forma as adjusted net tangible book value of $ per ordinary share to existing shareholders, and an immediate dilution in the pro forma as adjusted net tangible book value of $ per ordinary share to investors purchasing ordinary shares in this offering. The following table illustrates this per ordinary share dilution on a per ordinary share basis:

<table>
<thead>
<tr>
<th>Assumed initial public offering price per ordinary share</th>
<th>$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Historical net tangible book deficit per ordinary share as of December 31, 2017</td>
<td>$</td>
</tr>
<tr>
<td>Increase per ordinary share attributable to the pro forma adjustments described above</td>
<td>$</td>
</tr>
<tr>
<td>Pro forma net tangible book value per ordinary share as of December 31, 2017</td>
<td>$</td>
</tr>
<tr>
<td>Increase in pro forma as adjusted net tangible book value per ordinary share attributable to this offering</td>
<td>$</td>
</tr>
<tr>
<td>Pro forma as adjusted net tangible book value per ordinary share after this offering</td>
<td>$</td>
</tr>
<tr>
<td>Dilution per ordinary share to investors purchasing ordinary shares in this offering</td>
<td>$</td>
</tr>
</tbody>
</table>

Each $1.00 increase or decrease in the assumed initial public offering price of $ per ordinary 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 $ per ordinary share, and the dilution per ordinary share to investors purchasing ordinary shares in this offering by $ per ordinary share, assuming that the number of ordinary 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 ordinary 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 ordinary share after this offering by $ per ordinary share and decrease the dilution to investors purchasing ordinary shares in this offering by $ per ordinary share, assuming no change in the assumed initial public offering price per ordinary share and after deducting estimated underwriting discounts and commissions. Each decrease of 1.0 million in the number of ordinary 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 ordinary share after this offering by $\_\_\_\_\_\_\_\_\_\_\_ per ordinary share and increase the dilution to investors purchasing ordinary shares in this offering by $\_\_\_\_\_\_\_\_\_\_\_ per ordinary share, assuming no change in the assumed initial public offering price per ordinary share and after deducting estimated underwriting discounts and commissions.

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

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

<table>
<thead>
<tr>
<th>Shares purchased</th>
<th>Total consideration</th>
<th>Weighted average price per ordinary share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>Percent</td>
<td>Amount</td>
</tr>
<tr>
<td>Existing shareholders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Investors in this offering</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Each $\_\_\_\_\_\_\_\_\_\_ increase or decrease in the assumed initial public offering price of $\_\_\_\_\_\_\_\_\_\_ per ordinary 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 ordinary shares in this offering by $\_\_\_\_\_\_\_\_\_\_\_ million, and in the case of an increase, would increase the percent of total consideration paid by new investors by percentage points, and in the case of a decrease, would decrease the percent of total consideration paid by new investors by percentage points, assuming that the number of ordinary 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 ordinary 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 ordinary shares in this offering by $\_\_\_\_\_\_\_\_\_\_\_ million and, in the case of an increase, would increase the percentage of total consideration paid by investors purchasing ordinary shares in this offering by percentage points and, in the case of a decrease, would decrease the percentage of total consideration paid by investors purchasing ordinary shares in this offering by percentage points, assuming no change in the assumed initial public offering price per ordinary share.

If the underwriters exercise their option in full to purchase additional ordinary shares in this offering, the number of ordinary shares held by existing shareholders will be reduced to % of the total number of ordinary shares to be outstanding after this offering, and the number of ordinary shares held by investors participating in this offering will be increased to % of the total number of ordinary shares to be outstanding after this offering.
The total number of ordinary shares reflected in the discussion and tables above is based on ordinary shares outstanding as of December 31, 2017, and excludes:

- ordinary shares issuable upon the exercise of share options outstanding under our 2015 Plan as of December 31, 2017, at a weighted-average exercise price of $ per ordinary share;

- ordinary shares reserved and available for future issuance under our 2015 Plan as of December 31, 2017; and

- ordinary shares 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 ordinary shares reserved for issuance under our 2018 Plan.

To the extent that options are exercised, new options or other equity awards are issued under our equity incentive plans, or we issue additional ordinary shares in the future, there will be further dilution to investors purchasing ordinary shares in this offering. Assuming the exercise of all of our outstanding options as of December 31, 2017, the number of ordinary shares held by existing shareholders would increase to % of the total number of ordinary shares to be outstanding after this offering, and the number of ordinary shares held by investors participating in this offering would be reduced to % of the total number of ordinary shares to be outstanding after this offering. Additionally, the total consideration paid to us by existing shareholders would be $ million, or %, of the total consideration paid for our outstanding ordinary shares, and the total consideration paid to us by investors participating in this offering would be % of the total consideration paid for our outstanding shares. The weighted average price per ordinary share paid to us by existing shareholders would be $ and the weighted average price per ordinary 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 shareholders.
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 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 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.

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>(in thousands, except share and per share data)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Consolidated Statement of Operations Data:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating expenses:</td>
</tr>
<tr>
<td>Research and development</td>
</tr>
<tr>
<td>General and administrative</td>
</tr>
<tr>
<td>Total operating expenses</td>
</tr>
<tr>
<td>Loss from operations</td>
</tr>
<tr>
<td>Other income:</td>
</tr>
<tr>
<td>Interest income</td>
</tr>
<tr>
<td>Total other income</td>
</tr>
<tr>
<td>Net loss</td>
</tr>
<tr>
<td>Net loss per share—basic and diluted(1)</td>
</tr>
<tr>
<td>Weighted-average ordinary shares outstanding—basic and diluted(1)</td>
</tr>
<tr>
<td>Pro forma net loss per share(1)</td>
</tr>
<tr>
<td>Pro forma weighted-average ordinary shares outstanding—basic and diluted(1)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>As of December 31,</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>(in thousands)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Consolidated Balance Sheet Data:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash and cash equivalents</td>
</tr>
<tr>
<td>Total assets</td>
</tr>
<tr>
<td>Total liabilities</td>
</tr>
<tr>
<td>Redeemable convertible preference shares</td>
</tr>
<tr>
<td>Total shareholders' deficit</td>
</tr>
</tbody>
</table>
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 two lead product candidates, ETX2514 and ETX0282, inhibit one of the most prevalent forms of bacterial resistance, b-lactamase enzymes, so-named because of their ability to inactivate b-lactam antibiotics, one of the most commonly used classes of antibiotics. By blocking this resistance mechanism, these product candidates, when administered in combination with b-lactam antibiotics, are designed to restore the efficacy of those antibiotics. ETX2514 is a novel broad-spectrum intravenous, or IV, b-lactamase inhibitor, or BLI, that we are developing in combination with sulbactam, an IV b-lactam antibiotic, for the treatment of a variety of serious multi-drug resistant infections caused by Acinetobacter baumannii, or Acinetobacter. We have completed a Phase 1 clinical trial and, based on a series of discussions with the U.S. Food and Drug Administration, or FDA, we plan to move ETX2514SUL into a single Phase 3 clinical trial in the first quarter of 2019. To optimize the Phase 3 clinical trial, we are conducting additional Phase 1 clinical trials and plan to initiate a Phase 2 clinical trial in the first quarter of 2018. We expect to receive data from these Phase 1 and Phase 2 clinical trials by the end of 2018. ETX0282 is a novel oral BLI that we are developing in combination with cefpodoxime proxetil, an oral b-lactam antibiotic, for the treatment of complicated urinary tract infections, or UTIs, including those caused by extended-spectrum b-lactamase, or ESBL, – producing bacterial strains or carbapenem-resistant Enterobacteriaceae, or CRE. We believe there is a significant unmet need for new oral antibiotics that reliably treat patients with multi-drug resistant Gram-negative infections. We believe our preclinical data supports progression to a multi-part Phase 1 clinical trial for ETX0282, which we anticipate initiating in the second quarter of 2018.

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. Through December 31, 2017, we have funded our operations primarily from the sale of our preference shares 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 non-profit awards from the Drugs for Neglected Diseases initiative, or DNDi.

Since our inception, we have incurred significant operating losses. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current or future product candidates and programs. Our net loss was $19.1 million for the year ended December 31, 2016. As of December 31, 2016, we
had an accumulated deficit of $27.2 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 closing 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.

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 December 31, 2016, we have not received any cash or recognized any 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.

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” for additional information.
**Components of Results of Operations**

**Revenue**

To date, we have not generated any revenue from any sources, including 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 or license or collaboration agreements with third parties, 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 incurred in connection 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 includes 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. These employees work across multiple programs and, therefore, we do not track their costs by program.

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

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The table shows our research and development expenses by development program and type of activity for the year ended December 31, 2016:

<table>
<thead>
<tr>
<th>Year Ended December 31, 2016</th>
<th>(in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Direct research and development expenses by program:</strong></td>
<td></td>
</tr>
<tr>
<td>ETX2514</td>
<td>$ 4,661</td>
</tr>
<tr>
<td>ETX0282</td>
<td>2,162</td>
</tr>
<tr>
<td>Zoliflodacin</td>
<td>744</td>
</tr>
<tr>
<td>Other preclinical programs</td>
<td>562</td>
</tr>
<tr>
<td><strong>Unallocated research and development expenses:</strong></td>
<td></td>
</tr>
<tr>
<td>Personnel expenses (including share-based compensation)</td>
<td>5,314</td>
</tr>
<tr>
<td>Facilities, supplies and other</td>
<td>2,335</td>
</tr>
<tr>
<td><strong>Total research and development expenses</strong></td>
<td>$ 15,778</td>
</tr>
</tbody>
</table>

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.

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General and Administrative Expenses

General and administrative expenses consist primarily of salaries and benefits, travel and share-based compensation expense for personnel in executive, finance and administrative functions. General and administrative costs 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.

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.

Results of Operations

Year Ended December 31, 2016

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

<table>
<thead>
<tr>
<th>Description</th>
<th>Year Ended December 31, 2016 (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating expenses:</td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>$15,778</td>
</tr>
<tr>
<td>General and administrative</td>
<td>3,326</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>19,104</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(19,104)</td>
</tr>
<tr>
<td>Other income:</td>
<td></td>
</tr>
<tr>
<td>Interest income</td>
<td>9</td>
</tr>
<tr>
<td>Total other income</td>
<td>9</td>
</tr>
<tr>
<td>Net loss</td>
<td>$ (19,095)</td>
</tr>
</tbody>
</table>

Research and Development Expenses

<table>
<thead>
<tr>
<th>Description</th>
<th>Year Ended December 31, 2016 (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personnel expenses (including share-based compensation)</td>
<td>$5,314</td>
</tr>
<tr>
<td>Preclinical and development expenses</td>
<td>8,129</td>
</tr>
<tr>
<td>Facilities and supplies</td>
<td>1,825</td>
</tr>
<tr>
<td>Other expenses</td>
<td>510</td>
</tr>
<tr>
<td></td>
<td>$15,778</td>
</tr>
</tbody>
</table>
Research and development expenses were $15.8 million for the year ended December 31, 2016. During 2016, we continued to execute on our strategy by advancing the clinical development of our lead product candidates; ETX2514 was moved into a multi-part Phase 1 clinical trial and ETX0282 was moved into preclinical development. Our research and development expenses for the year ended December 31, 2016 included personnel expenses of $5.3 million, which included share-based compensation expense of $0.2 million. Preclinical and development expenses of $8.1 million for the period included manufacturing costs of $4.4 million, which were primarily related to drug production for our ETX2514 Phase 1 clinical trial and drug production for ETX0282, payments to external contractors of $1.4 million, primarily associated with ETX0282 and other preclinical programs, clinical trial costs of $1.3 million primarily related to the Phase 1 clinical trial of ETX2514, and preclinical study costs of $1.0 million primarily associated with ETX2514 and ETX0282. Facilities allocation and supplies expenses of $1.8 million included $1.3 million related to the allocation of facilities costs, mostly pertaining to our office and laboratory lease, and $0.5 million related to laboratory supplies. Other expenses of $0.5 million primarily consisted of professional fees of $0.3 million. We anticipate research and development costs will increase in the future as we continue to advance the clinical development of our product candidates and our preclinical programs.

**General and Administrative Expenses**

<table>
<thead>
<tr>
<th>Category</th>
<th>Amount (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personnel expenses (including share-based compensation)</td>
<td>$1,909</td>
</tr>
<tr>
<td>Legal and professional fees</td>
<td>1,189</td>
</tr>
<tr>
<td>Other expenses</td>
<td>228</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3,326</strong></td>
</tr>
</tbody>
</table>

General and administrative expenses were $3.3 million for the year ended December 31, 2016. During 2016, we continued to develop our administrative process infrastructure, expand our intellectual property portfolio and further develop our corporate governance processes. Our general and administrative personnel expenses of $1.9 million included share-based compensation expense of $0.4 million. Legal and professional fees of $1.2 million included corporate and patent legal costs of $0.6 million and consulting costs of $0.4 million, as we had no legal or finance employees during 2016.

**Income Taxes**

There was no provision for income taxes for the year ended December 31, 2016 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 December 31, 2017, we have raised aggregate net cash proceeds of $104.2 million from the sale of redeemable convertible preference shares, 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 A preference shares 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 B redeemable convertible preference shares. In August 2017, we received net proceeds of $24.4 million from the sale of 42,372,882 B-1 redeemable convertible preference shares and in December 2017, we
received net cash proceeds of $31.9 million from the closing of the sale of 54,067,796 B-1 redeemable convertible preference shares. 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 non-profit awards from DNDi. As of December 31, 2017, we had cash and cash equivalents of $ 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 for the year ended December 31, 2016 and, as of December 31, 2016, we had an accumulated deficit of $27.2 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 into . We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect.

**Funding Requirements**

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

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

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

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

As a result, we will need substantial additional funding to support our continuing operations and 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 shareholder. Debt financing and preference 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 costs and expenses for fees to 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 period presented:

<table>
<thead>
<tr>
<th>Year Ended December 31, 2016 (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net cash used in operating activities</td>
</tr>
<tr>
<td>Net cash used in investing activities</td>
</tr>
<tr>
<td>Net cash provided by financing activities</td>
</tr>
<tr>
<td>Net increase in cash and cash equivalents</td>
</tr>
</tbody>
</table>

Operating Activities

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 costs and associated drug manufacturing costs for the advancement of ETX2514 and ETX0282, our lead product candidates. We utilized a number of third-party vendors to support our development programs in 2016 and expect to continue to do so in future years. As our product candidates progress to later stages of development, we expect that our external expenditures will continue to increase.

Investing Activities

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 year ended December 31, 2016, net cash provided by financing activities was $42.2 million, which related to sales of redeemable convertible preference shares. In March 2016, we issued and sold 25,000,000 B redeemable convertible preference shares 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 A redeemable convertible preference shares, which amount was held by AstraZeneca pursuant to our cash management services arrangement.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2016:

<table>
<thead>
<tr>
<th>Payments Due by Period</th>
<th>Total (in thousands)</th>
<th>Less than 1 Year</th>
<th>1 to 3 Years</th>
<th>4 to 5 Years</th>
<th>More than 5 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating lease commitments(1)</td>
<td>$ 1,313</td>
<td>$ 376</td>
<td>$ 791</td>
<td>$ 146</td>
<td>$ —</td>
</tr>
<tr>
<td>Total</td>
<td>$ 1,313</td>
<td>$ 376</td>
<td>$ 791</td>
<td>$ 146</td>
<td>$ —</td>
</tr>
</tbody>
</table>

(1) Amounts in the table reflect minimum payments due for our lease with AstraZeneca for office and laboratory space, which extends through May 2020 and includes certain renewal periods.
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 year ended December 31, 2016, 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.

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...
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.

Share-Based Compensation

We measure share-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 share-based awards with service-based vesting conditions and record the expense for these awards using the straight-line method.

For share-based awards granted to consultants and non-employees, we recognize 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 is re-measured using the then-current fair value of our ordinary shares and updated assumption inputs in the Black-Scholes option-pricing model.

We estimate the fair value of each share option grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our ordinary shares and assumptions we make for the expected term of our share options, the volatility of our ordinary shares, which is based on the historical volatility of publicly traded peer companies for the expected term of our share options, the risk-free interest rate for a period that approximates the expected term of our share options and our expected dividend yield.

Valuation of Ordinary Shares

As there has been no public market for our ordinary shares to date, the estimated fair value of our ordinary shares 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 ordinary shares as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third-party valuation through the date of the grant. 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 ordinary shares valuations were prepared using the option-pricing method, or OPM, which used a market approach to estimate our enterprise value. The OPM treats ordinary shares and preference shares as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities
Under this method, the ordinary shares have value only if the funds available for distribution to shareholders exceeded the value of the preference shares. Liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger. A discount for lack of marketability of the ordinary shares is then applied to arrive at an indication of value for the ordinary shares. These third-party valuations were performed at various dates, which resulted in valuations of our ordinary shares of $0.18 per share as of May 31, 2016 and December 31, 2016. Our board of directors considered various objective and subjective factors to determine the fair value of our ordinary shares as of each grant date, including:

- any recent valuations of our ordinary shares 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 preference shares to outside investors in arm's length transactions and the rights, preferences and privileges of the redeemable convertible preference shares relative to those of our ordinary shares, including the liquidation preferences of the redeemable convertible preference shares;
- the illiquid nature of our ordinary shares;
- 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 ordinary shares, 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 ordinary shares based on the closing price of our ordinary shares 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 underlying ordinary shares and the associated per-share exercise price, which was the fair value per share as determined by our board of

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directors on the applicable grant date, for share options granted during the year ended December 31, 2016:

<table>
<thead>
<tr>
<th>Grant Date</th>
<th>Number of Ordinary Shares-Subject to Options Granted</th>
<th>Exercise Price per Ordinary Share</th>
<th>Estimated Fair Value per Ordinary Share at Grant Date</th>
<th>Estimated Per-Share Fair Value of Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>October 21, 2016</td>
<td>3,752,683</td>
<td>$0.18</td>
<td>$0.18</td>
<td>$0.10</td>
</tr>
<tr>
<td>October 21, 2016</td>
<td>175,032</td>
<td>0.18</td>
<td>0.18</td>
<td>0.12</td>
</tr>
</tbody>
</table>

The intrinsic value of all outstanding options as of December 31, 2017 was $\text{X}$ million, based on the estimated fair value of our ordinary shares of $\text{Y}$ per share, the midpoint of the price range set forth on the cover page of this prospectus, of which approximately $\text{Z}$ million related to vested options and approximately $\text{W}$ 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 December 31, 2016 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 two lead product candidates, ETX2514 and 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 first product candidate, 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 a Phase 1 clinical trial and, based on a series of discussions with the U.S. Food and Drug Administration, or FDA, we plan to move ETX2514SUL into a single Phase 3 clinical trial in the first quarter of 2019. To optimize the Phase 3 clinical trial, we are conducting additional Phase 1 clinical trials and plan to initiate a Phase 2 clinical trial in the first quarter of 2018. We expect to receive data from these Phase 1 and Phase 2 clinical trials by the end of 2018.

Our second product candidate, ETX0282CPDP, is an oral, fixed-dose combination of ETX0282, a novel oral BLI, with cefpodoxime proxetil, an oral β-lactam antibiotic, which we are developing 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. We believe there is a significant unmet need for new oral antibiotics that reliably treat patients with multi-drug resistant Gram-negative infections. We believe our preclinical data supports progression to a multi-part Phase 1 clinical trial of ETX0282, which we anticipate initiating in the second quarter of 2018. We expect to receive data from the single-ascending dose escalation part of the trial in the fourth quarter of 2018, and the remainder of the data in the first half of 2019. In addition to our two lead product candidates, we are also developing zoliflodacin, a novel orally administered product candidate that targets bacterial gyrase for the treatment of drug-resistant Neisseria gonorrhoeae, the bacterial pathogen responsible for gonorrhea. We have completed a Phase 2 clinical trial of zoliflodacin and intend to initiate a Phase 3 clinical trial in 2019. The Phase 3 clinical trial is being funded by our non-profit collaborator, the Drugs for Neglected Diseases initiative, or DNDi.

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.

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, 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:

<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Upcoming Milestones</th>
<th>Commercial Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETX2514SUL</td>
<td>Multi-drug resistant Aerobacter infections</td>
<td>* Initiate Phase 3 trial in Q 2019&lt;sup&gt;1&lt;/sup&gt;, data expected in 2020</td>
<td>Worldwide</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| ETX282CPD1        | Carbapenem-resistant infections (Pseudomonas, CRE and others) | * Initiate Phase 2 trial in Q 2018; data expected by the end of 2019<sup>2</sup> | Worldwide |

| Zoliflodacin      | Uncomplicated gonorrhea | * Initiate Phase 3 trial in 2019 | All developed countries<sup>3</sup> |

| NDP Program       | Gram-negative infections (initially multi-drug resistant Pseudomonas) | * Select initial clinical candidate in 2019 | Worldwide |

<sup>1</sup> We have completed a Phase 1 clinical trial and, 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.

<sup>2</sup> Safety and pharmacokinetic data from the Phase 2 trial will be used to support the NDA package for ETX2514SUL.
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 in which ETX2514 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 initiated two additional Phase 1 clinical trials to evaluate drug penetration into the lung and to assess pharmacokinetics in renally impaired patients. In parallel with these additional Phase 1 clinical trials, we have also chosen to conduct a Phase 2 clinical trial in patients with complicated UTIs to provide additional safety and pharmacokinetic data as well as efficacy data against carbapenem-resistant pathogens. We expect to receive top-line data from these Phase 1 and Phase 2 clinical trials by the end of 2018. 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 Primaxin™ in our clinical trials to provide broad coverage for these other pathogens. Primaxin is an FDA-approved fixed-dose combination of imipenem, a carbapenem antibiotic, and cilastatin, a drug that prevents degradation of imipenem. Throughout our clinical trials, we plan to collect data on the activity of ETX2514SUL in combination with Primaxin against a range of Gram-negative pathogens in addition to *Acinetobacter*. Based on the results of our preclinical studies, 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.
**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 3.5 million to 4.5 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-lactam 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 anticipate initiating a multi-part Phase 1 clinical trial of ETX0282 in Australia in the second quarter of 2018. We expect to receive data from the single-ascending dose escalation part of the trial in the fourth quarter of 2018 and the remainder of the data in the first half of 2019.

**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.

**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 two lead product candidates, ETX2514SUL and ETX0282CPDP, 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 initiate a multi-part Phase 1 clinical trial of ETX0282 in the second quarter of 2018. We expect to receive data from the single-ascending dose escalation part of the trial in the fourth quarter of 2018 and the remainder of the data in the first half of 2019. We also plan to explore additional indications with these product candidates. For example, based on the results of our preclinical studies, 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 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. We plan to initiate a Phase 3 clinical trial in 2019, which will be fully funded by DNDi. 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.

• **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 nonprofit organizations, government agencies and other third parties, including DNDi, 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, 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 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. Approximately 60% of hospital-treated infections are Gram-negative.

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.

- **Cidal activity:** 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$_{90}$, these data represent the MIC associated with inhibiting the growth of at least 90% 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.

### B-lactam Antibiotics

b-lactams are one of the most widely used antibiotic classes due to their attractive safety and efficacy profile. b-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. b-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. b-lactam antibiotics consist of all antibiotic agents that contain a b-lactam ring in their molecular structures. Among b-lactam antibiotics, penicillin derivatives and cephalosporins are the most commonly used. Carbapenems, another class of b-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 b-lactam antibiotics by synthesizing b-lactamases, enzymes that attack the b-lactam ring. b-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 b-lactamases, clavulanic acid could restore the potency of b-lactam agents. One of the most commercially successful antibiotics, Augmentin™, is a combination of amoxicillin, a b-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 b-lactamases, including Class C b-lactamases and Class A carbapenemases. In response to the increasing number of b-lactamases, biopharmaceutical companies developed additional IV BLIs that inhibit a broad-spectrum of Class A and Class C b-lactamases, enabling the restoration of the antibacterial activity of the b-lactam antibiotics with which they are combined. While these newer BLIs represent a significant step forward, they do not broadly inhibit Class D b-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 b-lactamase coverage for the treatment of infections caused by multi-drug resistant *Acinetobacter*. Using our targeted-design platform, we engineered ETX2514 to expand the b-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 b-lactamases.

We selected sulbactam as the b-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 b-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 b-lactamase-mediated resistance rendered sulbactam generally ineffective. We believe that ETX2514’s expanded coverage against Classes A, C and D b-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 Primaxin 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, 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 Phase 1 clinical trial at doses that are well in excess of our expected Phase 3 clinical trial dose. 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, 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 at least 128 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 Primaxin or colistin plus Primaxin over a period of up to 14 days. Primaxin is an FDA-approved fixed-dose combination of imipenem, a carbapenem antibiotic, and cilastatin, a drug that prevents degradation of imipenem. The primary endpoint will be 28-day all-cause mortality, with a 19% non-inferiority margin, in the approximately 128 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 Primaxin 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 Primaxin. 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. We plan to initiate the Phase 3 clinical trial during the first quarter of 2019 and expect to receive data in 2020.

We have employed rigorous pharmacokinetic and pharmacodynamic modeling to project the efficacious ETX2514SUL dosing regimen. Our analyses suggest a 1.0 g dose of ETX2514 combined with 1.0 g sulbactam infused over 3 hours every 6 hours will deliver a therapeutically active dose in patients. Data from our additional ongoing Phase 1 clinical trials and planned Phase 2 clinical trial will also be incorporated into this analysis to further refine dose setting ahead of the Phase 3 clinical trial.

Additional Ongoing and Planned Clinical Trials

To optimize our Phase 3 clinical trial, we have initiated two additional Phase 1 clinical trials in the United States to evaluate drug penetration into the lung and to assess pharmacokinetics in renally impaired patients. The lung trial will assess the concentration of ETX2514SUL in lung fluid, which is important 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. The renal trial will analyze serum levels in renally impaired patients and provide a dose-adjustment protocol for these types of patients, who are also likely to be enrolled in the Phase 3 clinical trial. We expect to receive data from these Phase 1 clinical trials by the end of 2018.
In parallel with these additional Phase 1 clinical trials, we have also chosen to conduct 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. The Phase 2 clinical trial is designed as a 2:1 randomized, 80-patient trial comparing ETX2514SUL plus Primaxin to placebo plus Primaxin. 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 ETX2514 to restore the activity of imipenem against multiple other bacterial pathogens, such as CRE and carbapenem-resistant Pseudomonas. We believe this may allow us to expand the clinical utility of ETX2514SUL. We plan to initiate this trial in the first quarter of 2018 and expect to receive data by the end of 2018.

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 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 Primaxin, 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 Primaxin, infused every 6 hours over a period of 11 days, was generally well tolerated.

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 ongoing Phase 1 clinical trials are being conducted in the United States under this IND. The FDA granted Fast Track designation and QIDP designation for ETX2514SUL in September 2017.

Preclinical Data

We designed ETX2514 to achieve broad activity against a wide range of b-lactamases, including Classes A, C and D, unlike currently marketed BLIs that primarily cover only Class A and Class C b-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
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

In Vivo Activity of ETX2514 + Sulbactam in Mouse Lung Infection Model

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 2,177 recent strains of *Acinetobacter*. The plot in the figure below presents the cumulative percentage of these 2,177 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 2,177 Acinetobacter Strains**

![In Vitro Activity of ETX2514SUL Against 2,177 Acinetobacter Strains](image)

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC$_{90}$ (mg/L)</th>
<th>CLSI Breakpoint (mg/L)</th>
</tr>
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<tr>
<td>Sulbactam</td>
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<td>ETX2514SUL</td>
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<td>Imipenem</td>
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<td>Meropenem</td>
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<tr>
<td>Amikacin</td>
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<tr>
<td>Colistin</td>
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</table>

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

In this study, the 2 mg/L MIC$_{90}$ of ETX2514SUL was equivalent to colistin, which also had a 2 mg/L MIC$_{90}$ against these 2,177 *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, the broad-spectrum carbapenem component of Primaxin. 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 MIC₉₀ 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 Primaxin 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.

<table>
<thead>
<tr>
<th>MIC₉₀ (mg/L)</th>
<th>E. coli 262 strains</th>
<th>Klebsiella 199 strains</th>
<th>Pseudomonas 1,202 strains</th>
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<tr>
<td>Imipenem</td>
<td>0.25</td>
<td>1</td>
<td>16</td>
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<tr>
<td>ETX2514 + Imipenem</td>
<td>≤0.06</td>
<td>0.12</td>
<td>2</td>
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</table>

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 expect to initiate 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 3.5 million to 4.5 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 b-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 b-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 b-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 b-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 3.5 million to 4.5 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 anticipate initiating a multi-part Phase 1 clinical trial of ETX0282CPDP in Australia in the second quarter of 2018. The Phase 1 clinical trial will be 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 total, we anticipate enrolling approximately 116 healthy volunteers in the Phase 1
clinical trial. Data from the trial will support dose selection for our subsequent clinical trials. We expect to receive data from the single-ascending dose escalation part of the trial in the fourth quarter of 2018 and the remainder of the data in the first half of 2019. In parallel with the Phase 1 clinical trial, we plan to conduct a pre-IND meeting with the FDA to discuss 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:

<table>
<thead>
<tr>
<th>Prodrug</th>
<th>Active Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-lactam</td>
<td></td>
</tr>
<tr>
<td>Cefpodoxime proxetil (CPDP)</td>
<td>Cefpodoxime (CPD)</td>
</tr>
<tr>
<td>β-lactamase inhibitor</td>
<td>ETX0282</td>
</tr>
<tr>
<td></td>
<td>ETX1317</td>
</tr>
</tbody>
</table>

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 three 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, and to fosfomycin and trimethoprim/sulfamethoxazole, other commonly used oral antibiotics. 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\textsubscript{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\textsubscript{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

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

**MIC\(_{90}\) was not determined for trimethoprim / sulfamethoxazole at the concentrations tested (0.5 mg/L and 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\(^{\text{TM}}\) and Avycaz\(^{\text{TM}}\), 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.

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\(^{(1)}\) ETX0282CPDP is an oral prodrug which is metabolized into ETX1317, the active BLI, and cefpodoxime.

\(^{(2)}\) MIC\(_{90}\) was not determined for trimethoprim / sulfamethoxazole at the concentrations tested (0.5 mg/L and 4 mg/L).
ETX0282CPDP(1) 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 b-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.

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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. We believe that the results of these studies are supportive of progression of ETX0282 to the clinic.

**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 1.1 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. 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 patients with uncomplicated gonorrhea who will be randomized on a 2:1 basis to receive either a single oral dose of zoliflodacin or a single intramuscular dose of ceftriaxone. 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 will be 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 and Phase 2 clinical trials were, and the planned Phase 3 trial will be, conducted pursuant to an IND submitted to the FDA in August 2013 by AstraZeneca.

**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 MIC90 values are much higher than the susceptibility breakpoints for each.
In Vitro Activity of Oral Zoliflodacin Against 250 N. Gonorrhoeae Strains

<table>
<thead>
<tr>
<th></th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt; (mg/L)</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt; (mg/L)</th>
<th>CLSI Breakpoint (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zoliflodacin (Oral)</td>
<td>0.25</td>
<td>0.25</td>
<td>NA</td>
</tr>
<tr>
<td>Ciprofloxacin (Oral)</td>
<td>&gt;32</td>
<td>&gt;32</td>
<td>0.06</td>
</tr>
<tr>
<td>Azithromycin (Oral)</td>
<td>4</td>
<td>&gt;32</td>
<td>0.25&lt;sup&gt;1)&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cefixime (Oral)</td>
<td>0.25</td>
<td>4</td>
<td>0.25</td>
</tr>
<tr>
<td>Ceftriaxone (intramuscular)</td>
<td>0.12</td>
<td>2</td>
<td>0.25</td>
</tr>
</tbody>
</table>

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

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 b-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 b-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.
Through December 31, 2017, 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. The A preference shares will automatically be converted into ordinary shares 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 ordinary shares 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 shareholders 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, our ordinary shares, or a combination of cash and our ordinary shares. 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. 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.

**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 ceftiderocol, currently in a Phase 3 clinical trial, from Shionogi & Co., Ltd.

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 plazomicin. 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 SPR994 from Spero Therapeutics Inc., currently in a Phase 1 clinical trial.

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.

**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 October 3, 2017, we owned two issued U.S. patents, seven issued foreign patents as well as 33 pending foreign patent applications and one pending Patent Cooperation Treaty, or PCT. The issued foreign patents are in a number of jurisdictions including the Australia, China, Japan, New Zealand, 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.

**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 October 3, 2017, we owned one pending foreign patent application in Taiwan and one pending PCT. Issued U.S. and foreign patents and patents issuing from pending U.S. and foreign applications will have expiration dates of September 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 October 3, 2017, we owned five issued U.S. patents, 15 issued foreign patents as well as 38 pending foreign patent applications. The issued foreign patents are in a number of jurisdictions, including the European Union, Eurasia, Australia, Canada, China, Hong Kong, Japan, South Africa, South Korea, Mexico and New Zealand. 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.

**Provisional Patents**

In addition to the issued and pending patent applications covering our most advanced product candidates, our portfolio also includes three provisional patent applications relating to our early-stage discovery projects.
Patent Term and Term Extensions

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is twenty years from the earliest effective filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or the USPTO, in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug or biological product may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date of a U.S. patent as partial compensation for the length of time the drug is under regulatory review while the patent is in force. A patent term extension cannot extend the remaining term of a patent beyond a total of fourteen years from the date of product approval, only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. We cannot provide any assurance that any patent term extension with respect to any U.S. patent will be obtained and, if obtained, the duration of such extension.

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

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

Intellectual Property from the Collaboration with 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.
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 a 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. 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

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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.
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 healthcare program 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 healthcare program 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 healthcare program anti-kickback statute has been violated. Additionally, the intent standard under the federal healthcare program 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

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including items or services resulting from a violation of the federal healthcare program 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 new 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 healthcare program 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 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 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 to report annually 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. 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% 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;
- creation of the Independent Payment Advisory Board, which, if and when impaneled, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs; 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. The Trump administration has also announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for the CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments has been introduced in the Senate, but the future of that bill is uncertain. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, each chamber of Congress has put forth multiple bills this year designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, 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, providers are subject to Medicare payment reductions of 2% per fiscal year through 2025 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 proposed bills 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.

Individual states in the United States have also 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. 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 December 1, 2017, we had 30 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 12,805 square feet of leased office, research and development and laboratory facility space in Waltham, Massachusetts, pursuant to a lease agreement that expires in May 2020, with an option to extend the term of the lease for an additional three years. 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:

<table>
<thead>
<tr>
<th>Name</th>
<th>Age</th>
<th>Position</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Executive Officers:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manoussos Perros, Ph.D.</td>
<td>50</td>
<td>President, Chief Executive Officer and Director</td>
</tr>
<tr>
<td>Michael Gutch, Ph.D.</td>
<td>51</td>
<td>Chief Financial Officer and Chief Business Officer</td>
</tr>
<tr>
<td>Robin Isaacs, M.D.</td>
<td>59</td>
<td>Chief Medical Officer</td>
</tr>
<tr>
<td>John Mueller, Ph.D.</td>
<td>57</td>
<td>Chief Development Officer</td>
</tr>
<tr>
<td>Ruben Tommasi, Ph.D.</td>
<td>52</td>
<td>Chief Scientific Officer</td>
</tr>
<tr>
<td><strong>Non-Management Directors:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicholas Galakatos, Ph.D.</td>
<td>60</td>
<td>Chairman of the Board of Directors</td>
</tr>
<tr>
<td>Heather Behanna, Ph.D.</td>
<td>42</td>
<td>Director</td>
</tr>
<tr>
<td>Thomas Dyrbeg, M.D., D.M.Sc.*</td>
<td>63</td>
<td>Director</td>
</tr>
<tr>
<td>Robert Hopfner, Ph.D.</td>
<td>45</td>
<td>Director</td>
</tr>
<tr>
<td>Gregory Norden</td>
<td>60</td>
<td>Director</td>
</tr>
<tr>
<td>Heather Preston, M.D.</td>
<td>51</td>
<td>Director</td>
</tr>
<tr>
<td>Andrew J. Staples</td>
<td>48</td>
<td>Director</td>
</tr>
<tr>
<td>James N. Topper, M.D., Ph.D.</td>
<td>55</td>
<td>Director</td>
</tr>
</tbody>
</table>

* Dr. Dyrbeg 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. Nuvolution 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 since January 2017, focusing on biopharmaceutical investments. Prior to joining Sofinnova, 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.

Robert Hopfner, Ph.D., has been a member of our board of directors since December 2017. Dr. Hopfner has served as a managing director and 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, Univation 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. Since 2005, Dr. Preston has served as a managing director at TPG BioTech, a biotechnology venture capital firm. 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 Albireo Pharma, Inc., Alder BioPharmaceuticals, Inc., Otonomy, Inc. and a number of private companies. 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 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.

Board Composition

Our board of directors currently consists of nine members. Our board of directors will consist of eight members following the resignation of Dr. Dyrberg 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 preference shares. 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 articles of association, which will be in effect upon the closing 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 general meeting, 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 , and , and their term will expire at our first general meeting to be held after the completion of this offering;

• Class II, which will consist of , and , and their term will expire at our second general meeting to be held after the completion of this offering;

• Class III, which will consist of , and , and their term will expire at our third general meeting to be held after the completion of this offering.

Our amended and restated articles of association, which will be in effect upon the closing 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 consist of directors, and , and , 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. is the chairman of the audit committee and our board of directors has determined that 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, subject to shareholder approval, 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 consist of directors, , and , each of whom is a non-employee member of our board of directors as defined in Rule 16b-3 under the Exchange Act. 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 share 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 directors, , and . 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.entasisrx.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.

**Insurance and Indemnification**

To the extent permitted by the U.K. Companies Act 2006, or the Companies Act, we are empowered to indemnify our directors against any liability they incur by reason of their directorship. We maintain directors’ and officers’ insurance to insure such persons against certain liabilities. We expect to enter into an indemnification agreement with each of our directors and executive officers prior to the completion of this offering.

In addition to such indemnification, we provide our directors and executive officers with directors’ and officers’ liability insurance.

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.

<table>
<thead>
<tr>
<th>Name and Principal Position</th>
<th>Year</th>
<th>Salary ($)</th>
<th>Bonus ($)</th>
<th>Option Awards ($)</th>
<th>All Other Compensation ($)</th>
<th>Total ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manoussos Perros, Ph.D.</td>
<td>2017</td>
<td>429,867</td>
<td>—</td>
<td>341,416</td>
<td>8,100(4)</td>
<td>779,383</td>
</tr>
<tr>
<td>President and Chief Executive Officer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Michael Gutch, Ph.D.(6)</td>
<td>2017</td>
<td>228,750</td>
<td>—</td>
<td>140,453</td>
<td>67,654(5)</td>
<td>436,857</td>
</tr>
<tr>
<td>Chief Financial Officer and Chief Business Officer</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robin Isaacs, M.D.</td>
<td>2017</td>
<td>383,760</td>
<td>—</td>
<td>49,131</td>
<td>8,100(4)</td>
<td>440,991</td>
</tr>
<tr>
<td>Chief Medical Officer</td>
<td>2016</td>
<td>372,000</td>
<td>160,233</td>
<td>37,835</td>
<td>119,765(7)</td>
<td>664,833</td>
</tr>
</tbody>
</table>

(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. The bonus payments to our named executive officers for 2017 have not yet been determined. We expect that they will be determined in the first quarter of 2018.

(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 share options, the exercise of the share options or the sale of the ordinary shares underlying such share 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 shareholders, 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:

<table>
<thead>
<tr>
<th>Name</th>
<th>2017 Base Salaries</th>
<th>2018 Base Salaries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manoussos Perros, Ph.D.</td>
<td>$432,640</td>
<td>$</td>
</tr>
<tr>
<td>Michael Gutch, Ph.D.</td>
<td>$305,000</td>
<td>$</td>
</tr>
<tr>
<td>Robin Isaacs, M.D.</td>
<td>$385,632</td>
<td>$</td>
</tr>
</tbody>
</table>

(1) The 2018 base salaries of our named executive officers have not yet been determined. We expect that they will be determined in the first quarter of 2018.

**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.

**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 share options qualifying as incentive share options, non-qualified share options, restricted share awards, restricted share units and other share-based awards.
We typically grant share options at the start of employment to each executive and our other employees. Through 2017, we have not maintained a practice of granting additional equity on an annual basis, but we have retained discretion to provide additional targeted grants in appropriate circumstances.

We award share 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 share options to Dr. Gutch upon commencement of his employment with us. Dr. Gutch received an option to purchase 851,294 ordinary shares with an exercise price of $0.18 per ordinary share. Of the shares underlying this option, 25% vests on April 1, 2018, and the remaining shares vest in 36 equal monthly installments thereafter. In November 2017, our board of directors awarded share options to each of our named executive officers. Drs. Perros, Gutch and Isaacs received an option to purchase 3,793,510 ordinary shares, 520,116 ordinary shares and 545,904 ordinary shares, respectively. Each of these options has an exercise price of $0.15 per ordinary 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 share options to each of our named executive officers. Drs. Perros and Isaacs received options to purchase 1,450,353 ordinary shares and 378,353 ordinary shares, respectively. Each of these options has an exercise price of $0.18 per ordinary 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.

Offer Letter Agreements and Potential Payments upon Termination of Employment or Change of Control

We have entered into offer letter agreements with each of our named executive officers. Furthermore, each of our named executive officers has executed a form of our standard confidentiality and proprietary rights agreement. The key terms of the offer letter agreements 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’ initial base salary was set at $400,000 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 our ordinary shares 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 1,812,941 ordinary shares 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.

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’s base salary was set at $305,000 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 of up to 35% of his 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 ordinary shares 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 851,294 ordinary shares 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.

**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' initial base salary was set at $360,000 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 ordinary shares 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 472,941 ordinary shares 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.

**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 share 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.

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.

<table>
<thead>
<tr>
<th>Name</th>
<th>Option Awards</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Securities Underlying Options Exercisable</td>
</tr>
<tr>
<td>Manoussos Perros, Ph.D.</td>
<td>1,170,858</td>
</tr>
<tr>
<td></td>
<td>634,529</td>
</tr>
<tr>
<td></td>
<td>—</td>
</tr>
<tr>
<td>Michael Gutch, Ph.D.</td>
<td>851,294(4)</td>
</tr>
<tr>
<td>Robin Isaacs, M.D.</td>
<td>285,735</td>
</tr>
<tr>
<td></td>
<td>165,529</td>
</tr>
<tr>
<td></td>
<td>—</td>
</tr>
</tbody>
</table>

(1) Of the ordinary shares underlying the option, 25% vested on May 13, 2016, and the remaining ordinary 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 ordinary shares underlying the option, 25% vested on March 29, 2017, and the remaining ordinary shares vest in 36 equal monthly installments thereafter, subject to the officer’s continued service through each vesting date.

(3) Of the ordinary 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 ordinary 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.

(5) Of the ordinary shares underlying the option, 25% vested on July 1, 2016, and the remaining ordinary shares vest in 36 equal monthly installments thereafter, subject to the officer’s continued service through each vesting date.

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

We expect that our board of directors will adopt, and our shareholders will approve, prior to the completion of this offering, our 2018 equity incentive plan, or our 2018 Plan. 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 ordinary shares have been issued under our 2018 Plan. Our 2018 Plan will provide for the grant of share 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 non-qualifying share options, or NSOs, restricted share awards, restricted share unit awards, share appreciation rights, performance share awards and other forms of share compensation to our employees, including officers, 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 maximum number of ordinary shares that may be issued under our 2018 Plan is ordinary shares. The number of ordinary shares 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 % of the total number of ordinary shares outstanding on December 31 of the preceding calendar year, or a lesser number of ordinary shares as may be determined by our board of directors. The maximum number of ordinary shares that may be issued pursuant to the exercise of ISOs under the 2018 Plan is .

Shares issued under our 2018 Plan may be authorized but unissued or reacquired ordinary shares. Ordinary shares subject to share 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 ordinary shares, will not reduce the number of ordinary shares available for issuance under our 2018 Plan. Additionally, ordinary shares issued pursuant to share awards under our 2018 Plan that we repurchase or that are forfeited, as well as ordinary shares reacquired by us as consideration for the exercise or purchase price of a share award or to satisfy tax withholding obligations related to a share 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 share awards and (ii) determine the number of ordinary shares to be subject to such share 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 share awards, if any, the number of shares subject to each share award, the fair market value of an ordinary share, 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 share 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 share appreciation right, cancel and re-grant any outstanding option or share appreciation right in exchange for new share 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.

Section 162(m) Limits

No participant may be granted share awards covering more than ordinary shares under our 2018 Plan during any calendar year pursuant to share options, share appreciation rights and other share awards whose value is determined by reference to an increase over an exercise price or strike price of at least 100% of the fair market value of our ordinary shares on the date of grant. Additionally, no participant may be granted in a calendar year a performance share award covering more than ordinary shares or a performance cash award having a maximum value in excess of under our 2018 Plan. These limitations enable us to grant awards that will be exempt from the $1,000,000 limitation on the income tax deductibility of compensation paid per covered executive officer imposed by Section 162(m) of the Code.

Performance Awards

Our 2018 Plan permits the grant of performance-based share and cash awards that may qualify as performance-based compensation that is not subject to the $1,000,000 limitation on the income tax deductibility of compensation paid per covered executive officer imposed by Section 162(m) of the Code. To enable us to grant performance-based awards that will qualify, our compensation committee can structure such awards so that the share or cash will be issued or paid pursuant to such award only following the achievement of specified pre-established performance goals during a designated performance period.

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, lease 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 at least 50% of the outstanding share capital of our company, the administrator will determine how to treat each outstanding share award. The administrator may:

• arrange for the assumption, continuation or substitution of a share 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 share 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; or
• cancel the share award prior to the transaction in exchange for a cash payment, which may be reduced by the exercise price payable in connection with the share award.

The administrator is not obligated to treat all share awards or portions of share 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 share 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 share award will be subject to additional acceleration of vesting and exercisability in the event of a change in control. In the absence of such a provision, no such acceleration of the share award will occur.

Plan 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

Our board of directors originally adopted and our shareholders approved the 2015 Plan in May 2015. The 2015 Plan was amended in September 2015, and was subsequently amended and restated in March 2016 and in August 2017. 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 share awards will be granted under the 2015 Plan. Upon the consummation of the corporate reorganization, our successor entity will assume the 2015 Plan.

Our 2015 Plan provides for the grant of ISOs, NSOs, share appreciation rights, restricted share awards, restricted share unit awards, phantom share and dividend equivalent rights, or collectively, share awards. ISOs may be granted only to our employees, including our officers, and the employees of our affiliates. All other share 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 ordinary shares that may be issued pursuant to share awards under our 2015 Plan is ________ shares. As of December 31, 2017, options to purchase ________ ordinary shares, at exercise prices ranging from $ ________ to $ ________ per ordinary share, were outstanding under our 2015 Plan.

Shares subject to share 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 has administered our 2015 Plan since its adoption. 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. Under our 2015 Plan, our board of directors has the authority to determine the terms of share 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 share award; and
- the form and terms and conditions of each share award.

Under 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.

Share Options

ISOs and NSOs are granted pursuant to option documents adopted by the plan administrator. The plan administrator determines the exercise price for share options, within the terms and conditions of our 2015 Plan, provided that the exercise price of a share option generally cannot be less than the greater of 100% of the fair market value of our ordinary shares on the date of grant or the nominal 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 ten 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 share 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 share awards.

Change of Control

Our 2015 Plan provides that in the event of a change in control transaction the plan administrator may take whatever action with respect to options and share 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. For this purpose, a change in control transaction includes: (1) a person obtaining control of our company within the meaning of section 719 of the UK Income Tax (Earnings and Pensions Act) 2003 either (i) following an offer to acquire the whole of our share capital, or (ii) on completion of a share sale and purchase agreement with our shareholders, or (iii) in any other circumstances or as a result of any other transaction or series of related transactions; (2) the consummation of a plan or other arrangement pursuant to which our company is dissolved or liquidated; (3) the sale or other disposition of all or substantially all of our assets, (4) the consummation of a merger or consolidation with or into another corporation, other than, in either case,
a merger or consolidation in which holders of ordinary shares immediately prior to the merger or consolidation will hold at least a majority of the ownership of ordinary shares of the surviving corporation immediately after the merger or consolidation, which ordinary shares (and, if applicable, voting securities) are to be held in the same proportion as such holders’ ownership of our ordinary shares immediately before the merger or consolidation and (5) the date any entity, person or group (other than (A) our company or any of our subsidiaries or any employee benefit plan (or related trust) sponsored or maintained by us or any of our subsidiaries or (B) any person who, on the date the 2015 Plan becomes effective, shall have been the beneficial owner of a majority of our outstanding ordinary shares and any affiliate of such person) becomes the beneficial owner of, or obtains voting control over, more than fifty percent (50%) of our outstanding ordinary shares. For purposes of this definition, “affiliate” means a person that directly, or indirectly through one or more intermediaries, controls, or is controlled by, or is under common control with, the referenced person.

Transferability

A participant generally may not transfer share 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 shareholder approval is required without obtaining such approval, or adversely affect the existing rights of any participant without such participant’s written consent. Certain material amendments also require the approval of our shareholders. No award may be granted after the tenth anniversary of the effective date of the 2015 Plan, which was May 11, 2015. No share awards may be granted under our 2015 Plan after it is terminated.

Non-Employee Director Compensation

We have not historically paid cash retainers or other compensation with respect to service on our board of directors, except for reimbursement of direct expenses incurred in connection with attending meetings of our board of directors or its committees. We expect that our board of directors will adopt a director compensation policy for non-employee directors to be effective following the completion of this offering.

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."

<table>
<thead>
<tr>
<th>Name</th>
<th>Option Awards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gregory Norden</td>
<td>$9,542</td>
</tr>
</tbody>
</table>

(1) This column reflects the aggregate grant date fair value of the option awards granted during fiscal year 2016 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 share options, the exercise of the share options or the sale of the ordinary shares underlying such share options.
(2) Represents an option to purchase 106,020 ordinary shares at an exercise price of $0.15 per ordinary share. Of the ordinary shares underlying this option, 25% will vest on August 25, 2018, and the remaining ordinary 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:

<table>
<thead>
<tr>
<th>Name</th>
<th>Option Awards Outstanding at Year-End</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gregory Norden</td>
<td>306,020</td>
</tr>
</tbody>
</table>

**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 ordinary shares on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from them. The director or officer 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 ordinary 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 ordinary 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.”

Transactions with AstraZeneca AB

In connection with our spin-out from AstraZeneca AB, or AstraZeneca, in May 2015, we issued 100 ordinary shares to AstraZeneca at a purchase price of $1.00 per ordinary share, for aggregate consideration of $100.

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 and the years ended December 31, 2016 and December 31, 2017, we paid rent of $0.2 million, $0.4 million and $0.6 million, respectively, under the lease agreement.

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.

<table>
<thead>
<tr>
<th>Purchaser</th>
<th>Number of B Preference Shares Purchased</th>
<th>Aggregate Purchase Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarus Lifesciences III, L.P. (1)</td>
<td>7,500,000</td>
<td>$7,500,000</td>
</tr>
<tr>
<td>Novo Holdings A/S (2)</td>
<td>7,000,000</td>
<td>7,000,000</td>
</tr>
<tr>
<td>Frazier Life Sciences VIII, L.P. (3)</td>
<td>7,000,000</td>
<td>7,000,000</td>
</tr>
<tr>
<td>Eventide Gilead Fund</td>
<td>3,062,500</td>
<td>3,062,500</td>
</tr>
<tr>
<td>Eventide Healthcare &amp; Life Science Fund</td>
<td>437,500</td>
<td>437,500</td>
</tr>
<tr>
<td>Total</td>
<td>25,000,000</td>
<td>$25,000,000</td>
</tr>
</tbody>
</table>

(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.

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

(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 partner and managing director of Pivotal bioVenture Partners.

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

(6) Heather Preston, a member of our board of directors, is a managing director 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 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 ”Ordinary Shares Eligible for Future Sale—Registration Rights.” The shareholders’ agreement will automatically terminate upon the closing 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 intend to enter into indemnification agreements with each of our directors and executive officers. These agreements and our articles of association 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—Insurance and Indemnification.”

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, 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 shareholder 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;

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- 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.
The following table sets forth the beneficial ownership of our ordinary shares as of December 31, 2017 for:

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our ordinary shares;
- 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 155,153,528 ordinary shares outstanding as of December 31, 2017, after giving effect to the automatic conversion of all of our outstanding preference shares into ordinary shares upon the closing of this offering. The percentage ownership information under the column titled "After Offering" is based on the sale of of our ordinary shares in this offering. The percentage ownership information assumes no exercise of the underwriters’ option to purchase additional ordinary 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 ordinary shares issuable pursuant to the exercise of share options that are exercisable on or before March 1, 2018, which is 60 days after December 31, 2017. These ordinary 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 ordinary shares shown as beneficially owned by them, subject to applicable community property laws.
<table>
<thead>
<tr>
<th>Name of Beneficial Owner</th>
<th>Number of Ordinary Shares Beneficially Owned Before Offering</th>
<th>Percentage of Ordinary Shares Beneficially Owned After Offering</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Principal Shareholders:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AstraZeneca AB(1)</td>
<td>33,500,000</td>
<td>21.6%</td>
</tr>
<tr>
<td>Clarus Lifesciences III, L.P.(2)</td>
<td>22,754,237</td>
<td>14.7</td>
</tr>
<tr>
<td>Novo Holdings A/S(3)</td>
<td>21,237,288</td>
<td>13.7</td>
</tr>
<tr>
<td>Frazier Life Sciences VIII, L.P.(4)</td>
<td>18,864,407</td>
<td>12.2</td>
</tr>
<tr>
<td>Pivotal bioVenture Partners Fund I, L.P.(5)</td>
<td>16,949,153</td>
<td>10.9</td>
</tr>
<tr>
<td>Sofinnova Venture Partners IX, L.P.(6)</td>
<td>16,949,153</td>
<td>10.9</td>
</tr>
<tr>
<td>TPG Biotechnology Partners V, L.P.(7)</td>
<td>15,254,237</td>
<td>9.8</td>
</tr>
<tr>
<td>Entities affiliated with Eventide Gilead Fund(8)</td>
<td>9,432,203</td>
<td>6.1</td>
</tr>
<tr>
<td><strong>Named Executive Officers and Directors:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manoussos Perros, Ph.D.(9)</td>
<td>1,941,358</td>
<td>1.2</td>
</tr>
<tr>
<td>Michael Gutch, Ph.D.(10)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Robin Isaacs, M.D.(11)</td>
<td>496,588</td>
<td>*</td>
</tr>
<tr>
<td>Nicholas Galakatos, Ph.D.(12)</td>
<td>22,754,237</td>
<td>14.7</td>
</tr>
<tr>
<td>Heather Behanna, Ph.D.(13)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Thomas Dyrberg, M.D., D.M.Sc.(14)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Robert Hopfner, Ph.D.(15)</td>
<td>16,949,153</td>
<td>10.9</td>
</tr>
<tr>
<td>Gregory Norden(16)</td>
<td>66,667</td>
<td>*</td>
</tr>
<tr>
<td>Heather Preston, M.D.(17)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Andrew J. Staples(18)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>James N. Topper, M.D., Ph.D.(19)</td>
<td>18,864,407</td>
<td>12.2</td>
</tr>
<tr>
<td>All current directors and executive officers as a group (13 persons)(20)</td>
<td>62,085,292</td>
<td>39.1</td>
</tr>
</tbody>
</table>

* Represents beneficial ownership of less than 1%.

(1) Consists of 100 ordinary shares and 33,499,900 ordinary shares issuable upon conversion of A preference shares. The principal business address of AstraZeneca AB is SE-151, 85 Sodertalje, Sweden.

(2) Consists of 7,500,000 ordinary shares issuable upon conversion of B preference shares and 15,254,237 ordinary shares issuable upon conversion of B-1 preference sRidershares. 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 LLC, or Clarus III GP LLC, 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 GP LLC. 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 GP LLC likewise may be deemed to own beneficially the shares held by Clarus III. As the managing directors of Clarus III GP LLC, 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 7,000,000 ordinary shares issuable upon conversion of B preference shares and 14,237,288 ordinary shares issuable upon conversion of B-1 preference shares. The board of directors of Novo Holdings A/S, or Novo, consists of Sten Scheibye, Göran Ando, Jeppe Christiansen, Steen Riisgaard, Per Wold-Olsen, 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 7,000,000 ordinary shares issuable upon conversion of B preference shares and 11,864,407 ordinary shares issuable upon conversion of B-1 preference shares. The general partner of Frazier Life Sciences VIII, L.P., or FLS L.P., is FHM Life Sciences VIII, L.P., 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 L.P. 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 L.P. is Two Union Square, 601 Union Street, Suite 3200, Seattle, WA 98101.

(5) Consists of 16,949,153 ordinary shares issuable upon conversion of B-1 preference shares. The general partner of Pivotal bioVenture Partners Fund I, L.P., or Pivotal, 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. Pivotal Partners Ltd is the sole shareholder of the Ultimate General Partner and voting and investment power with respect to the shares. The principal business address of Pivotal is 1700 Owens Street, Suite 595, San Francisco, CA 94158.

(6) Consists of 16,949,153 ordinary shares issuable upon conversion of B-1 preference shares. 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 15,254,237 ordinary shares issuable upon conversion of B-1 preference shares. 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) 3,062,500 ordinary shares issuable upon conversion of B preference shares and 5,190,678 ordinary shares issuable upon conversion of B-1 preference shares held by Eventide Gilead Fund and (ii) 437,500 ordinary shares issuable upon conversion of B preference shares and 741,525 ordinary shares issuable upon conversion of B-1 preference shares held by Eventide Healthcare & Life Science Fund. Eventide Gilead Fund and Eventide Healthcare & Life Science 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 1,941,358 ordinary shares issuable upon the exercise of outstanding options exercisable within 60 days of December 31, 2017.

(10) Dr. Gutch does not have any outstanding options exercisable within 60 days of December 31, 2017.

(11) Consists of 496,588 ordinary shares issuable upon the exercise of outstanding options exercisable within 60 days of December 31, 2017.

(12) Consists of 7,500,000 ordinary shares issuable upon conversion of B preference shares and 15,254,237 ordinary shares issuable upon conversion of B-1 preference shares. Clarus Ventures III GP, L.P., or Clarus III GP, is the sole general partner of Clarus III. Clarus III GPLLCC 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 GPLLCC. 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 GP, Clarus III GPLLCC likewise may be deemed to own beneficially the shares held by Clarus III. As the managing directors of Clarus III GPLLCC, each of the Managers 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. Dr. Behanna is not deemed to have any beneficial ownership or reportable pecuniary interest 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) Consists of 16,949,153 ordinary shares issuable upon conversion of B-1 preference shares held by Pivotal. Dr. Hopfner is a partner and managing director of Pivotal bioVenture Partners Management Ltd., or the Investment Advisor, which is the investment advisor to Pivotal, and is partner of Pivotal bioVenture Partners Investment Adviser 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.

(16) Consists of 66,667 ordinary shares issuable upon the exercise of outstanding options exercisable within 60 days of December 31, 2017.

(17) Dr. Preston is a managing director 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.

(18) 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.

(19) Consists of 7,000,000 ordinary shares issuable upon conversion of B preference shares and 11,864,407 ordinary shares issuable upon conversion of B-1 preference shares. 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.

(20) Consists of (i) 14,500,000 ordinary shares issuable upon conversion of B preference shares, (ii) 44,067,797 ordinary shares issuable upon conversion of B-1 preference shares and (iii) 3,517,495 ordinary shares issuable upon the exercise of outstanding options exercisable within 60 days of December 31, 2017.
DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION

The following describes our issued share capital, summarizes the material provisions of our Articles of Association and highlights certain differences in corporate law in the United Kingdom and the State of Delaware.

The newly formed Entasis Therapeutics Limited was incorporated as a private limited company pursuant to the laws of England and Wales on , 2018 for the purpose of becoming the holding company for EntasisTx Limited and Entasis Therapeutics, Inc. Pursuant to the terms of a corporate reorganization that will be completed prior to the closing of this offering, the shareholders of Entasis Therapeutics Limited will exchange the entire issued share capital of EntasisTx Limited for the same number and classes of the newly formed Entasis Therapeutics Limited and, as a result, EntasisTx Limited will become a wholly owned subsidiary of the newly formed Entasis Therapeutics Limited. Prior to the consummation of this offering, the newly formed Entasis Therapeutics Limited will re-register as a public limited company and change its name to Entasis Therapeutics plc, convert all of its outstanding shares into a single class of ordinary shares and complete a reverse share split. See the section titled "Corporate Reorganization" for more information.

We are registered with the Registrar of Companies in England and Wales under number 09475809, and our registered office is at 3rd floor, 1 Ashley Road, Altrincham, Cheshire WA14 2DT, United Kingdom. Our principal offices are at 35 Gatehouse Drive, Waltham, Massachusetts 02451.

Following our corporate reorganization, certain resolutions will be required to be passed by our shareholders prior to the completion of this offering. These will include resolutions for the:

• adoption of amended and restated articles of association that will become effective upon the completion of this offering. See the subsection titled "—Post-IPO Articles of Association" below;

• general authorization of our directors for purposes of Section 551 of the Companies Act to allot shares in the company and grant rights to subscribe for or convert any securities into shares in the company up to a maximum aggregate nominal amount of $ for a period of years; and

• empowering of our directors pursuant to Section 570 of Companies Act to allot equity securities for cash pursuant to the Section 551 authority referred to above as if the statutory preemption rights under Section 561(1) of the Companies Act did not apply to such allotments.

Issued Share Capital

As of December 31, 2017, our issued share capital was divided into ordinary shares held of record by shareholders, deferred shares held of record by shareholder, 33,499,900 A preference shares held of record by one shareholder, 25,000,000 B preference shares held of record by five shareholders and 96,440,678 B-1 preference shares held of record by eight shareholders. The nominal value of the ordinary shares is $0.20 each, the nominal value of the deferred shares is $0.20 each, the nominal value of the A preference shares and B preference shares is $1.00 each, and the nominal value of the B-1 preference shares is $0.59 each. All of the issued share capital is fully paid. Following the contemplated exchange of shares of the newly renamed EntasisTx Limited for shares of the newly formed Entasis Therapeutics Limited, the issued share capital of Entasis Therapeutics Limited will comprise the same number and class of shares. As of the completion of the corporate reorganization and this offering, our issued share capital will be ordinary shares with a nominal value of $ per ordinary share.
Ordinary Shares

In accordance with our amended and restated articles of association to be in effect upon the completion of this offering, the following summarizes the rights of holders of our ordinary shares:

• each holder of our ordinary shares is entitled to one vote per ordinary share on all matters to be voted on by shareholders generally;

• the holders of the ordinary shares shall be entitled to receive notice of, attend, speak and vote at our general meetings; and

• holders of our ordinary shares are entitled to receive such dividends as are recommended by our directors and declared by our shareholders.

Registered Shares

We are required by the Companies Act to keep a register of our shareholders. Under English law, the ordinary shares are deemed to be issued when the name of the shareholder is entered in our share register. The share register therefore is prima facie evidence of the identity of our shareholders, and the shares that they hold. The share register generally provides limited, or no, information regarding the ultimate beneficial owners of our ordinary shares. Our share register is maintained by our registrar.

Under the Companies Act, we must enter an allotment of shares in our share register as soon as practicable and in any event within two months of the allotment. We will perform all procedures necessary to update the share register to reflect the ordinary shares being sold in this offering. We also are required by the Companies Act to register a transfer of shares (or give the transferee notice of and reasons for refusal as the transferee may reasonably request) as soon as practicable and in any event within two months of receiving notice of the transfer.

We, any of our shareholders or any other affected person may apply to the court for rectification of the share register if:

• the name of any person, without sufficient cause, is wrongly entered in or omitted from our register of members; or

• there is a default or unnecessary delay in entering on the register the fact of any person having ceased to be a member or on which we have a lien, provided that such delay does not prevent dealings in the shares taking place on an open and proper basis.

Preemption Rights

English law generally provides shareholders with preemption rights when new shares are allotted for cash; however, it is possible for shareholders of a public limited company to disapply these statutory preemption rights by special resolution in a general meeting. Such a disapplication of pre-emption rights may be for a maximum period of up to five years from the date of the shareholder resolution. Any disapplication of pre-emption rights must be renewed by shareholders prior to its expiration. On , our shareholders approved a general authority for the board of directors to allot shares for cash for a period of five years from the date of approval and the disapplication of pre-emption rights in respect any such allotments, which disapplication will need to be renewed upon expiration (i.e., five years from the date of approval) to remain effective, but may be sought more frequently for additional five-year terms (or any shorter period). On , our shareholders also approved the disapplication of pre-emption rights in respect of the allotment of ordinary shares in connection with this offering.
Post-IPO Articles of Association

Our articles of association, or the articles, were adopted by a special resolution of the shareholders on [date]. A summary of the terms of the articles is set out below. The summary below is not a complete description of the terms of the articles.

The articles contain no specific restrictions on our purpose and therefore, by virtue of section 31(1) of the Companies Act, our purpose is unrestricted.

The articles contain, among other things, provisions to the following effect:

Share Capital

Our share capital currently consists of [number] ordinary shares. We may issue shares with such rights or restrictions as may be determined by ordinary resolution, including shares which are to be redeemed, or are liable to be redeemed at our option or the holder of such shares.

Voting

The shareholders have the right to receive notice of, and to vote at, our general meetings. Each shareholder who is present in person (or, being a corporation, by representative) at a general meeting on a show of hands has one vote and, on a poll, every such holder who is present in person (or, being a corporation, by representative) or by proxy has one vote in respect of every share held by him.

Variation of Rights

Whenever our share capital is divided into different classes of shares, the special rights attached to any class may be varied or abrogated either with the consent in writing of the holders of three-fourths in nominal value of the issued shares of that class or with the sanction of a special resolution passed at a general meeting of the holders of the shares of that class and may be so varied and abrogated whilst the company is a going concern.

Dividends

We may, subject to the provisions of the Companies Act and the articles, by ordinary resolution from time to time declare dividends to be paid to shareholders not exceeding the amount recommended by our board of directors. Subject to the provisions of the Companies Act, in so far as, in the board of directors' opinions, our profits justify such payments, the board of directors may pay interim dividends on any class of our shares.

Any dividend unclaimed after a period of 12 years from the date such dividend was declared or became payable shall, if the board of directors resolve, be forfeited and shall revert to us. No dividend or other money payable on or in respect of a share shall bear interest as against us.

Transfer of Ordinary Shares

Each member may transfer all or any of his shares which are in certificated form by means of an instrument of transfer in any usual form or in any other form which the board of directors may approve. Each member may transfer all or any of his shares which are in uncertificated form by means of a "relevant system" (i.e., the CREST System) in such manner provided for, and subject as provided in, the CREST Regulations.

The Board may, in its absolute discretion, refuse to register a transfer of certificated shares unless:

(i) it is for a share which is fully paid up;

(ii) it is for a share upon which the company has no lien;
it is only for one class of share;

(iv) it is in favor of a single transferee or no more than four joint transferees;

(v) it is duly stamped or is duly certificated or otherwise shown to the satisfaction of the board of directors to be exempt from stamp duty; and

(vi) it is delivered for registration to the registered office of the company (or such other place as the board of directors may determine), accompanied (except in the case of a transfer by a person to whom the company is not required by law to issue a certificate and to whom a certificate has not been issued or in the case of a renunciation) by the certificate for the shares to which it relates and such other evidence as the board of directors may reasonably require to prove the title of the transferor (or person renouncing) and the due execution of the transfer or renunciation by him or, if the transfer or renunciation is executed by some other person on his behalf, the authority of that person to do so.

The board of directors may refuse to register a transfer of uncertificated shares in any circumstances that are allowed or required by the CREST Regulations and the CREST System.

**Allotment of Shares and Preemption Rights**

Subject to the Companies Act and to any rights attached to existing shares, any share may be issued with or have attached to it such rights and restrictions as the company may by ordinary resolution determine, or if no ordinary resolution has been passed or so far as the resolution does not make specific provision, as the board of directors may determine (including shares which are to be redeemed, or are liable to be redeemed at the option of the company or the holder of such shares).

In accordance with section 551 of the Companies Act, the board of directors may be generally and unconditionally authorized to exercise all the powers of the company to allot shares up to an aggregate nominal amount equal to the amount stated in the relevant ordinary resolution authorizing such allotment.

The provisions of section 561 of the Companies Act (which confer on shareholders rights of preemption in respect of the allotment of equity securities which are paid up in cash) apply to the company except to the extent disappplied by special resolution of the company. Such preemption rights have been disappplied pursuant to the special resolution passed on .

**Alteration of Share Capital**

The company may by ordinary resolution consolidate or divide all of its share capital into shares of larger nominal value than its existing shares, or cancel any shares which, at the date of the ordinary resolution, have not been taken or agreed to be taken by any person and diminish the amount of its share capital by the nominal amount of shares so cancelled or sub-divide its shares, or any of them, into shares of smaller nominal value.

The company may, in accordance with the Companies Act, reduce or cancel its share capital or any capital redemption reserve or share premium account in any manner and with and subject to any conditions, authorities and consents required by law.

**Board of Directors**

Unless otherwise determined by the company by ordinary resolution, the number of directors (other than any alternate directors) shall not be less than two, but there shall be no maximum number of directors.
Subject to the articles and the Companies Act, the company may by ordinary resolution appoint a person who is willing to act as a director and the board of
directors shall have power at any time to appoint any person who is willing to act as a director, in both cases either to fill a vacancy or as an addition to the
existing board of directors.

Our articles provide that upon 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 general
meeting, 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.

At every subsequent annual general meeting any director who either (i) has been appointed by the board of directors since the last annual general meeting or
(ii) was not appointed or reappointed at one of the preceding two annual general meetings, must retire from office and may offer themselves for reappointment by
the shareholders by ordinary resolution.

Subject to the provisions of the articles, the board of directors may regulate their proceedings as they deem appropriate. A director may, and the secretary at
the request of a director shall, call a meeting of the directors.

The quorum for a meeting of the board of directors shall be fixed from time to time by a decision of the board of directors, but it must never be less than two
and unless otherwise fixed, it is two.

Questions and matters requiring resolution arising at a meeting shall be decided by a majority of votes of the participating directors, with each director
having one vote. In the case of an equality of votes, the chairman will only have a casting vote or second vote when an acquisition has been completed. The
entering into any acquisition requires the consent of 75% of the directors present and entitled to vote.

Directors shall be entitled to receive such remuneration as the board shall determine for their services to the company as directors, and for any other service
which they undertake for the company provided that the aggregate fees payable to the directors must not exceed $            per annum. The directors shall also be
entitled to be paid all reasonable expenses properly incurred by them in connection with their attendance at meetings of shareholders or class meetings, board of
director or committee meetings or otherwise in connection with the exercise of their powers and the discharge of their responsibilities in relation to the company.

The board of directors may, in accordance with the requirements in the articles, authorize any matter proposed to them by any director which would, if not
authorized, involve a director breaching his duty under the Companies Act, to avoid conflicts of interests.

A director seeking authorization in respect of such conflict shall declare to the board of directors the nature and extent of his interest in a conflict as soon as
is reasonably practicable. The director shall provide the board with such details of the matter as are necessary for the board to decide how to address the conflict
together with such additional information as may be requested by the board.

Any authorization by the board of directors will be effective only if:

(i) to the extent permitted by the Companies Act, the matter in question shall have been proposed by any director for consideration in the same way
that any other matter may be proposed to the directors under the provisions of the articles;

(ii) any requirement as to the quorum for consideration of the relevant matter is met without counting the conflicted director and any other conflicted
director; and

(iii) the matter is agreed to without the conflicted director voting or would be agreed to if the conflicted director's and any other interested director's
vote is not counted.
Subject to the provisions of the Companies Act, every director, secretary or other officer of the company (other than an auditor) is entitled to be indemnified against all costs, charges, losses, damages and liabilities incurred by him in the actual purported exercise or discharge of his duties or exercise of his powers or otherwise in relation to them.

**General Meetings**

The company must convene and hold annual general meetings in accordance with the Companies Act. Under the Companies Act, an annual general meeting must be called by notice of at least 21 days.

No business shall be transacted at any general meeting unless a quorum is present when the meeting proceeds to business, but the absence of a quorum shall not preclude the choice or appointment of a chairman of the meeting which shall not be treated as part of the business of the meeting. Save as otherwise provided by the articles, two shareholders present in person or by proxy and entitled to vote shall be a quorum for all purposes.

(i) **Borrowing Powers**

Subject to the articles and the Companies Act, the board of directors may exercise all of the powers of the company to:

(a) borrow money;

(b) indemnify and guarantee;

(c) mortgage or charge;

(d) create and issue debentures and other securities; and

(e) give security either outright or as collateral security for any debt, liability or obligation of the company or of any third party.

(ii) **Capitalization of profits**

The directors may, if they are so authorized by an ordinary resolution of the shareholders, decide to capitalize any undivided profits of the company (whether or not they are available for distribution), or any sum standing to the credit of the company’s share premium account or capital redemption reserve. The directors may also, subject to the aforementioned ordinary resolution, appropriate any sum which they so decide to capitalize to the persons who would have been entitled to it if it were distributed by way of dividend and in the same proportions.

(iii) **Uncertificated Shares**

Subject to the Companies Act, the board of directors may permit title to shares of any class to be issued or held otherwise than by a certificate and to be transferred by means of a "relevant system" (i.e., the CREST System) without a certificate.

The board of directors may take such steps as it sees fit in relation to the evidencing of and transfer of title to uncertificated shares, any records relating to the holding of uncertificated shares and the conversion of uncertificated shares to certificated shares, or vice-versa.

The company may by notice to the holder of an uncertificated share, require that share to be converted into certificated form.

The board of directors may take such other action that the board considers appropriate to achieve the sale, transfer, disposal, forfeiture, re-allotment or surrender of an uncertified share or otherwise to enforce a lien in respect of it.

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**Mandatory Bid**

(i) We believe that as of the date of this prospectus our place of central management and control is in the United Kingdom for the purposes of the jurisdictional criteria of the Takeover Code. Accordingly, we believe that we are currently subject to the Takeover Code and, as a result, our shareholders are currently entitled to the benefit of certain takeover offer protections provided under the Takeover Code, including the rules regarding mandatory takeover bids.

The Takeover Code provides a framework within which takeovers of companies are regulated and conducted. The Takeover Panel will, at any relevant time, review our place of central management and control based on the jurisdictional criteria of the Takeover Code, and their assessment as to jurisdiction may or may not change. Absent a relevant event occurring under the Takeover Code, it is unlikely that the Takeover Panel would re-assess jurisdiction in the interim. It is feasible that, in the future, due to changes in the board's composition, location of board meetings, the Takeover Panel's interpretation of the Takeover Code or other events, the Takeover Panel's assessment of its jurisdiction regarding and applicability of the Takeover Code to the Company may change.

Under the Takeover Code, where:

(a) any person, together with persons acting in concert with him, acquires, whether by a series of transactions over a period of time or not, an interest in shares which (taken together with shares in which he is already interested, and in which persons acting in concert with him are interested) carry 30% or more of the voting rights of a company; or

(b) any person who, together with persons acting in concert with him, is interested in shares which in the aggregate carry not less than 30% of the voting rights of a company but does not hold shares carrying more than 50% of such voting rights and such person, or any person acting in concert with him, acquires an interest in any other shares which increases the percentage of shares carrying voting rights in which he is interested;

such person shall, except in limited circumstances, be obliged to extend offers, on the basis set out in Rules 9.3, 9.4 and 9.5 of the Takeover Code, to the holders of any class of equity share capital, whether voting or non-voting, and also to the holders of any other class of transferable securities carrying voting rights. Offers for different classes of equity share capital must be comparable; the Takeover Panel should be consulted in advance in such cases.

(ii) An offer made under Rule 9 of the Takeover Code must, in respect of each class of shares involved, be in cash and at not less than the highest price paid by the person required to make an offer or any person acting in concert with him for any interest in the shares of that class during the 12 months prior to the announcement of the offer.

(iii) Under the Takeover Code, persons acting in concert comprise persons who, pursuant to an agreement or understanding (whether formal or informal and whether or not in writing) co-operate to obtain or consolidate control of a company. "Control" means an interest or interests in shares carrying 30% or more of the voting rights of a company, irrespective of whether the interest or interests give de facto control.

**Squeeze-out**

(i) Under sections 979 to 982 of the Companies Act, if an offeror, by virtue of acceptances of a takeover offer, were to acquire, or unconditionally contract to acquire, not less than 90% in value of the ordinary shares of the company and not less than 90% of the voting rights carried by those shares, it may compulsorily acquire the remaining 10%. It would do so by sending a
notice to outstanding shareholders telling them that it will compulsorily acquire their shares, provided that no such notice may be served after the end of: (a) the period of three months beginning with the day after the last day on which the offer can be accepted; or (b) if earlier, and the offer is not one to which section 943(1) of the Companies Act applies, the period of six months beginning with the date of the offer.

(ii) Six weeks following service of the notice, the offeror must send a copy of it to the company together with the consideration for the ordinary shares to which the notice relates, and an instrument of transfer executed on behalf of the outstanding shareholder(s) by a person appointed by the offeror.

(iii) The company will hold the consideration on trust for the outstanding shareholders.

Sell-out

(i) Sections 983 to 985 of the Companies Act give minority shareholders in the company a right to be bought out in certain circumstances by an offeror who has made a takeover offer. If a takeover offer relating to all the ordinary shares of the company is made at any time before the end of the period within which the offer could be accepted and the offeror has, by virtue of acceptances of the offer, acquired or unconditionally contracted to acquire not less than 90% in value of the ordinary shares of the company and not less than 90% of the voting rights carried by those shares, any holder of shares to which the offer related who had not accepted the offer may by a written communication to the offeror require it to acquire those shares. The offeror is required to give any shareholder who has not accepted the offer notice of his right to be bought out within one month of that right arising. The offeror may impose a time limit on the rights of minority shareholders to be bought out, but that period cannot end less than three months after the end of the acceptance period, or, if longer a period of three months from the date of the notice.

(ii) If a shareholder exercises his sell-out rights, the offeror is bound to acquire those shares on the terms of the offer or on such other terms as may be agreed.

Differences in Corporate Law

The applicable provisions of the Companies Act differ from laws applicable to Delaware corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of the Companies Act applicable to us and the General Corporation Law of the State of Delaware relating to shareholders’ rights and protections. This summary is not intended to be a complete discussion of the respective rights and it is qualified in its entirety by reference to Delaware law and the laws of England and Wales.

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<tr>
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<th>ENGLAND AND WALES</th>
<th>DELAWARE</th>
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<tr>
<td>Number of Directors</td>
<td>Under the Companies Act, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.</td>
<td>Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws.</td>
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</table>
### Removal of Directors

**Under the Companies Act**, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided 28 clear days’ notice of the resolution has been given to the company and its shareholders. On receipt of notice of an intended resolution to remove a director, the company must forthwith send a copy of the notice to the director concerned. Certain other procedural requirements under the Companies Act must also be followed, such as allowing the director to make representations against his or her removal either at the meeting or in writing.

**Under Delaware law**, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (i) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, stockholders may effect such removal only for cause, or (ii) in the case of a corporation having cumulative voting, if less than the entire board of directors is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.

### Vacancies on the Board of Directors

Under English law, the procedure by which directors, other than a company’s initial directors, are appointed is generally set out in a company’s articles of association, provided that where two or more persons are appointed as directors of a public limited company by resolution of the shareholders, resolutions appointing each director must be voted on individually.

Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (i) otherwise provided in the certificate of incorporation or bylaws of the corporation or (ii) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.

### Annual General Meeting

Under the Companies Act, a public limited company must hold an annual general meeting in each six-month period following the company’s annual accounting reference date.

Under Delaware law, the annual meeting of stockholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws.
General Meeting

Under the Companies Act, a general meeting of the shareholders of a public limited company may be called by the directors.

Shareholders holding at least 5% of the paid-up capital of the company carrying voting rights at general meetings (excluding any paid up capital held as treasury shares) can require the directors to call a general meeting and, if the directors fail to do so within a certain period, may themselves convene a general meeting.

Notice of General Meetings

Under the Companies Act, at least 21 days' notice must be given for an annual general meeting and any resolutions to be proposed at the meeting. Subject to a company's articles of association providing for a longer period, at least 14 days' notice is required for any other general meeting of a public limited company. In addition, certain matters, such as the removal of directors or auditors, require special notice, which is 28 days' notice. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the members having a right to attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting.

Under Delaware law, special meetings of the stockholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.

Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour and purpose or purposes of the meeting.
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<th>Proxy</th>
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<th>DELAWARE</th>
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<td></td>
<td>Under the Companies Act, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.</td>
<td>Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.</td>
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<th>Preemption Rights</th>
<th>ENGLAND AND WALES</th>
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<td>Under the Companies Act, &quot;equity securities,&quot; being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution, referred to as &quot;ordinary shares,&quot; or (ii) rights to subscribe for, or to convert securities into, ordinary shares, proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act.</td>
<td>Under Delaware law, stockholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.</td>
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<th>Authority to Allot</th>
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<td>Under the Companies Act, the directors of a company must not allot shares or grant rights to subscribe for or convert any security into shares unless an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise, in each case in accordance with the provisions of the Companies Act.</td>
<td>Under Delaware law, if the corporation's charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. The board may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive.</td>
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<td><strong>ENGLAND AND WALES</strong></td>
<td><strong>DELAWARE</strong></td>
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<td>Under the Companies Act, any provision, whether contained in a company's articles of association or any contract or otherwise, that purports to exempt a director of a company, to any extent, from any liability that would otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company, is void. Any provision by which a company directly or indirectly provides an indemnity, to any extent, for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act, which provides exceptions for the company to (i) purchase and maintain insurance against such liability; (ii) provide a &quot;qualifying third party indemnity,&quot; or an indemnity against liability incurred by the director to a person other than the company or an associated company or criminal proceedings in which he is convicted; and (iii) provide a &quot;qualifying pension scheme indemnity,&quot; or an indemnity against liability incurred in connection with the company's activities as trustee of an occupational pension plan.</td>
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<td>Under Delaware law, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its stockholders for damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for:</td>
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<td>• any breach of the director's duty of loyalty to the corporation or its stockholders;</td>
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<td>• acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;</td>
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<td>• intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or</td>
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<td>• any transaction from which the director derives an improper personal benefit.</td>
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**Voting Rights**

**ENGLAND AND WALES**

Under English law, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or the company's articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act, a poll may be demanded by (i) not fewer than five shareholders having the right to vote on the resolution; (ii) any shareholder(s) representing not less than 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any voting rights attaching to treasury shares); or (iii) any shareholder(s) holding shares in the company conferring a right to vote on the resolution (excluding any voting rights attaching to treasury shares) being shares on which an aggregate sum has been paid up equal to not less than 10% of the total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll.

Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present, in person or by proxy, who, being entitled to vote, vote on the resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present, in person or by proxy, at the meeting.

**DELAWARE**

Delaware law provides that, unless otherwise provided in the certificate of incorporation, each stockholder is entitled to one vote for each share of capital stock held by such stockholder.
The Companies Act provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers. These arrangements require:

• the approval at a shareholders’ or creditors’ meeting convened by order of the court, of a majority in number of shareholders or creditors representing 75% in value of the capital held by, or debt owed to, the class of shareholders or creditors, or class thereof present and voting, either in person or by proxy; and

• the approval of the court.

Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires:

• the approval of the board of directors; and

• the approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of the corporation entitled to vote on the matter.
Under English law, a director owes various statutory and fiduciary duties to the company, including:

- to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole;
- to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company;
- to act in accordance with the company’s constitution and only exercise his powers for the purposes for which they are conferred;
- to exercise independent judgment;
- to exercise reasonable care, skill and diligence;
- not to accept benefits from a third party conferred by reason of his being a director or doing, or not doing, anything as a director; and
- to declare any interest that he has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.

Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interest of the stockholders.

Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its stockholders. The duty of care generally requires that a director acts in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation.
Stockholder Suits

Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company’s internal management. Notwithstanding this general position, the Companies Act provides that (i) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director’s negligence, default, breach of duty or breach of trust and (ii) a shareholder may bring a claim for a court order where the company’s affairs have been or are being conducted in a manner that is unfairly prejudicial to some of its shareholders.

Under Delaware law, a stockholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must:

- state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the plaintiff’s shares thereafter devolved on the plaintiff by operation of law; and

- allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the reasons for the plaintiff’s failure to obtain the action; or

- state the reasons for not making the effort.

Additionally, the plaintiff must remain a stockholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery.

Transfer Agent and Registrar of Shares

Our share register is currently maintained by . The share register reflects only record owners of our ordinary shares.

Nasdaq Global Market Listing

We intend to apply to list our ordinary shares on The Nasdaq Global Market under the trading symbol “ETTX.”
ORDINARY SHARES ELIGIBLE FOR FUTURE SALE

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

Based on the number of shares outstanding as of December 31, 2017, upon completion of this offering and assuming no exercise of the underwriters’ option to purchase additional ordinary shares, of our ordinary shares will be outstanding, assuming the issuance of ordinary shares offered by us in this offering and the automatic conversion of all outstanding preference shares into ordinary shares upon the closing of this offering. All of the ordinary shares sold in this offering will be freely tradable without restrictions or further registration under the Securities Act, except for any shares sold to our “affiliates,” as that term is defined under Rule 144 under the Securities Act of 1933, as amended, or the Securities Act. The remaining ordinary shares held by existing shareholders 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 shares sold in this offering and of the existing restricted shares will be eligible for immediate sale upon the completion of this offering;

• approximately restricted shares will be eligible for sale in the public market 90 days after the date of this prospectus, subject to the volume, manner of sale and other limitations under Rule 144 and Rule 701; and

• approximately 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 ordinary shares for at least six months, and any affiliate of the company who owns either restricted or unrestricted ordinary shares, 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 ordinary shares then outstanding, which will equal approximately \( \frac{1}{100} \times 3,672,724 \) shares immediately after the completion of this offering based on the number of shares outstanding as of December 31, 2017; or
- the average weekly trading volume of our ordinary shares 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 December 31, 2017, we had outstanding options to purchase \( 3,672,724 \) of our ordinary shares. 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 ordinary shares that are issuable pursuant to our 2015 Plan and 2018 Plan. 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 our ordinary shares 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 ordinary shares, any options or warrants to purchase ordinary shares, or any securities convertible into, or exchangeable for or that represent the right to
receive ordinary shares, 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

We and the holders of our existing preference shares entered into an amended and restated shareholders' agreement in August 2017. The registration rights provisions of this agreement provide those holders with registration rights with respect to the ordinary shares that will be issued to them upon the automatic conversion of their preference shares at the completion of this offering. These registration rights include the right to demand registration of the holders' ordinary shares on up to two registration statements on Form S-1 and unlimited registration statements on Form S-3, as well as piggyback registration rights which will allow the holders to include their ordinary shares in any registration statement we file. We will generally be responsible for registration expenses in connection with the exercise of any of these registration rights. All of these registration rights are subject to specified conditions and limitations.
MATERIAL INCOME TAX CONSIDERATIONS

The following summary contains a description of material U.K. and U.S. federal income tax consequences of the acquisition, ownership and disposition of our ordinary shares. This summary should not be considered a comprehensive description of all the tax considerations that may be relevant to the decision to acquire ordinary shares in this offering.


The following is a description of the material U.S. federal income tax consequences to the U.S. Holders described below of owning and disposing of our ordinary shares. It is not a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire securities. This discussion applies only to a U.S. Holder that holds our ordinary shares as a capital asset for tax purposes (generally, property held for investment). In addition, it does not describe all of the tax consequences that may be relevant in light of a U.S. Holder's particular circumstances, including state and local tax consequences, estate tax consequences, alternative minimum tax consequences, the potential application of the Medicare contribution tax, and tax consequences applicable to U.S. Holders subject to special rules, such as:

- banks, insurance companies, and certain other financial institutions;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- persons holding ordinary shares as part of a hedging transaction, “straddle,” wash sale, conversion transaction or integrated transaction or persons entering into a constructive sale with respect to ordinary shares;
- persons whose “functional currency” for U.S. federal income tax purposes is not the U.S. dollar;
- brokers, dealers or traders in securities, commodities or currencies;
- tax-exempt entities or government organizations;
- S corporations, partnerships, or other entities or arrangements classified as partnerships for U.S. federal income tax purposes;
- regulated investment companies or real estate investment trusts;
- persons who acquired our ordinary shares pursuant to the exercise of any employee share option or otherwise as compensation;
- persons that own or are deemed to own 10 percent or more of our voting shares; and
- persons holding our ordinary shares in connection with a trade or business, permanent establishment, or fixed base outside the United States.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds ordinary shares, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships holding ordinary shares and partners in such partnerships are encouraged to consult their tax advisors as to the particular U.S. federal income tax consequences of holding and disposing of ordinary shares.

The discussion is based on the Code administrative pronouncements, judicial decisions, final, temporary and proposed Treasury Regulations, and the income tax treaty between the United Kingdom and the United States, or the Treaty, all as of the date hereof, changes to any of which may affect the tax consequences described herein—possibly with retroactive effect.

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A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of ordinary shares who is eligible for the benefits of the Treaty and is:

(i) a citizen or individual resident of the United States;

(ii) a corporation, or another entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;

(iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

(iv) 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 to be treated as a U.S. person under applicable U.S. Treasury Regulations.

U.S. Holders are encouraged to consult their tax advisers concerning the U.S. federal, state, local and foreign tax consequences of owning and disposing of ordinary shares in their particular circumstances.

**Passive Foreign Investment Company Rules**

If we are classified as a PFIC in any taxable year, a U.S. Holder will be subject to special rules generally intended to reduce or eliminate any benefits from the deferral of U.S. federal income tax that a U.S. Holder could derive from investing in a non-U.S. company that does not distribute all of its earnings on a current basis.

A non-U.S. corporation will be classified as a PFIC for any taxable year in which, after applying certain look-through rules, either:

- at least 75% of its gross income is passive income (such as interest income); or
- at least 50% of its gross assets (determined on the basis of a quarterly average) is attributable to assets that produce passive income or are held for the production of passive income.

We will be treated as owning our proportionate share of the assets and earning our proportionate share of the income of any other corporation, the equity of which we own, directly or indirectly, 25% or more (by value).

We believe that we were a PFIC for the calendar year ended December 31, 2016. Based on our estimates of expected gross assets and income, we believe that we will be classified as a PFIC for the year ending December 31, 2017. We cannot provide any assurances regarding our PFIC status for any past, current or future taxable year. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis and is based on principles and methodologies which in some circumstances are unclear and subject to varying interpretation.

A separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. As a result, our PFIC status may change from year to year. The total value of our assets for purposes of the asset test generally may be determined in part by reference to the market price of the ordinary shares, which may fluctuate considerably. Fluctuations in the market price of the ordinary shares may result in our being a PFIC for any taxable year. Because of the uncertainties involved in establishing our PFIC status, our United States tax counsel expresses no opinion regarding our PFIC status.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns the ordinary shares, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns the ordinary shares, regardless of whether we continue to
meet the tests described above unless (i) we cease to be a PFIC and the U.S. Holder has made a “deemed sale” election under the PFIC rules, or (ii) the U.S. Holder makes a Qualified Electing Fund Election, or QEF Election, with respect to all taxable years during such U.S. Holder's holding period in which we are a PFIC. We do not expect that a U.S. Holder will be eligible to make a QEF Election with respect to our ordinary shares. If the "deemed sale" election is made, a U.S. Holder will be deemed to have sold the ordinary shares the U.S. Holder holds at their fair market value and any gain from such deemed sale would be subject to the rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, the U.S. Holder's ordinary shares with respect to which such election was made will not be treated as shares in a PFIC and the U.S. Holder will not be subject to the rules described below with respect to any "excess distribution" the U.S. Holder receives from us or any gain from an actual sale or other disposition of the ordinary shares. U.S. Holders should consult their tax advisors as to the possibility and consequences of making a deemed sale election if such election becomes available.

For each taxable year we are treated as a PFIC with respect to U.S. Holders, U.S. Holders will be subject to special tax rules with respect to any "excess distribution" such U.S. Holder receives and any gain such U.S. Holder recognizes from a sale or other disposition (including a pledge) of ordinary shares, unless (i) such U.S. Holder makes a QEF Election or (ii) our ordinary shares constitute "marketable" securities, and such U.S. Holder makes a mark-to-market election as discussed below. Distributions a U.S. Holder receives in a taxable year that are greater than 125% of the average annual distributions a U.S. Holder received during the shorter of the three preceding taxable years or the U.S. Holder's holding period for the ordinary shares will be treated as an excess distribution. Under these special tax rules:

- the excess distribution or gain will be allocated ratably over a U.S. Holder's holding period for the ordinary shares;
- the amount allocated to the current taxable year, and any taxable year prior to the first taxable year in which we became a PFIC, will be treated as ordinary income in the current year; and
- the amount allocated to each other year will be subject to the highest tax rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years prior to the year of disposition or "excess distribution" cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of the ordinary shares cannot be treated as capital, even if a U.S. Holder holds the ordinary shares as capital assets.

If we are a PFIC, a U.S. Holder will generally be subject to similar rules with respect to distributions we receive from, and our dispositions of the shares of, any of our direct or indirect subsidiaries that also are PFICs, as if such distributions were indirectly received by, and/or dispositions were indirectly carried out by, such U.S. Holder. U.S. Holders should consult their tax advisors regarding the application of the PFIC rules to our subsidiaries.

U.S. Holders can avoid the interest charge on excess distributions or gain relating to the ordinary shares by making a mark-to-market election with respect to the ordinary shares, provided that the ordinary shares are "marketable." Ordinary shares will be marketable if they are "regularly traded" on certain U.S. stock exchanges or on a foreign stock exchange that meets certain conditions. For these purposes, the ordinary shares will be considered regularly traded during any calendar year during which they are traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. Any trades that have as their principal purpose meeting this requirement will be disregarded. Our ordinary shares will be listed on Nasdaq, which is a qualified exchange for these purposes. Consequently, if our ordinary shares remain listed on Nasdaq and are regularly traded, and you are a
holder of our ordinary shares, we expect the mark-to-market election would be available to U.S. Holders if we are a PFIC. Each U.S. Holder should consult its tax advisor as to whether a mark-to-market election is available or advisable with respect to the ordinary shares.

A U.S. Holder that makes a mark-to-market election must include in ordinary income for each year an amount equal to the excess, if any, of the fair market value of the ordinary shares at the close of the taxable year over the U.S. Holder's adjusted tax basis in the ordinary shares. An electing holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder's adjusted basis in the ordinary shares over the fair market value of the ordinary shares at the close of the taxable year, but this deduction is allowable only to the extent of any net mark-to-market gains for prior years. Gains from an actual sale or other disposition of the ordinary shares will be treated as ordinary income, and any losses incurred on a sale or other disposition of the shares will be treated as an ordinary loss to the extent of any net mark-to-market gains for prior years. Once made, the election cannot be revoked without the consent of the Internal Revenue Service, or the IRS, unless the ordinary shares cease to be marketable.

However, a mark-to-market election generally cannot be made for equity interests in any lower-tier PFICs that we own, unless shares of such lower-tier PFIC are themselves "marketable." As a result, even if a U.S. Holder validly makes a mark-to-market election with respect to our ordinary shares, the U.S. Holder may continue to be subject to the PFIC rules (described above) with respect to its indirect interest in any of our investments that are treated as an equity interest in a PFIC for U.S. federal income tax purposes. U.S. Holders should consult their tax advisors as to the availability and desirability of a mark-to-market election, as well as the impact of such election on interests in any lower-tier PFICs.

Unless otherwise provided by the U.S. Treasury, each U.S. shareholder of a PFIC is required to file an annual report containing such information as the U.S. Treasury may require. A U.S. Holder's failure to file the annual report will cause the statute of limitations for such U.S. Holder's U.S. federal income tax return to remain open with regard to the items required to be included in such report until three years after the U.S. Holder files the annual report, and, unless such failure is due to reasonable cause and not willful neglect, the statute of limitations for the U.S. Holder's entire U.S. federal income tax return will remain open during such period. U.S. Holders should consult their tax advisors regarding the requirements of filing such information returns under these rules.

**Taxation of Distributions**

Subject to the discussion above under "Passive Foreign Investment Company Rules," distributions paid on ordinary shares, other than certain pro rata distributions of ordinary shares, will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we may not calculate our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. Subject to applicable limitations, dividends paid to certain non-corporate U.S. Holders may be taxable at preferential rates applicable to "qualified dividend income." However, the qualified dividend income treatment may not apply if we are treated as a PFIC with respect to the U.S. Holder for the taxable year in which a dividend is paid or the preceding year. The amount of the dividend will be treated as foreign-source dividend income to U.S. Holders and will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code. Dividends will generally be included in a U.S. Holder's income on the date of the U.S. Holder's receipt of the dividend. The amount of any dividend income paid in foreign currency will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of actual or constructive receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain...
or loss if the dividend is converted into U.S. dollars after the date of receipt. Such gain or loss would generally be treated as U.S.-source ordinary income or loss. The amount of any distribution of property other than cash (and other than certain pro rata distributions of ordinary shares or rights to acquire ordinary shares) will be the fair market value of such property on the date of distribution.

For foreign tax credit limitation purposes, our dividends will generally be treated as passive category income. Because no U.K. income taxes will be withheld from dividends on ordinary shares, there will be no creditable foreign taxes associated with any dividends that a U.S. Holder will receive.

Sale or Other Taxable Disposition of Ordinary Shares

Subject to the discussion above under "Passive Foreign Investment Company Rules," gain or loss realized on the sale or other taxable disposition of ordinary shares will be capital gain or loss, and will be a long-term capital gain or loss if the U.S. Holder held the ordinary shares for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder's tax basis in the ordinary shares disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations.

If the consideration received by a U.S. Holder is not paid in U.S. dollars, the amount realized will be the U.S. dollar value of the payment received determined by reference to the spot rate of exchange on the date of the sale or other disposition. However, if the ordinary shares are treated as traded on an "established securities market" and you are either a cash basis taxpayer or an accrual basis taxpayer that has made a special election (which must be applied consistently from year to year and cannot be changed without the consent of the IRS), you will determine the U.S. dollar value of the amount realized in a non-U.S. dollar currency by translating the amount received at the spot rate of exchange on the settlement date of the sale. If you are an accrual basis taxpayer that is not eligible to or does not elect to determine the amount realized using the spot rate on the settlement date, you will recognize foreign currency gain or loss to the extent of any difference between the U.S. dollar amount realized on the date of sale or disposition and the U.S. dollar value of the currency received at the spot rate on the settlement date.

WE STRONGLY URGE YOU TO CONSULT YOUR TAX ADVISOR REGARDING THE IMPACT OF OUR PFIC STATUS ON YOUR INVESTMENT IN THE ORDINARY SHARES AS WELL AS THE APPLICATION OF THE PFIC RULES TO YOUR INVESTMENT IN THE ORDINARY SHARES.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (i) the U.S. Holder is a corporation or other exempt recipient or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding.

Backup withholding is not an additional tax. The amount of any backup withholding from a payment to a U.S. Holder will be allowed as a credit against the holder's U.S. federal income tax liability and may entitle it to a refund, provided that the required information is timely furnished to the IRS.

Information with Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals (and, under regulations, certain entities) may be required to report information relating to the ordinary shares, subject to certain exceptions (including an exception for ordinary shares held in accounts maintained by certain U.S. financial institutions). Such
U.S. Holders who fail to timely furnish the required information may be subject to a penalty. Additionally, if a U.S. Holder does not file the required information, the statute of limitations with respect to tax returns of the U.S. Holder to which the information relates may not close until three years after such information is filed. U.S. Holders should consult their tax advisers regarding their reporting obligations with respect to their ownership and disposition of the ordinary shares.

**U.K. Taxation**

The following is intended as a general guide to current U.K. tax law and HM Revenue & Customs, or HMRC, published practice applying as at the date of this prospectus (both of which are subject to change at any time, possibly with retrospective effect) relating to the holding of ordinary shares. It does not constitute legal or tax advice and does not purport to be a complete analysis of all U.K. tax considerations relating to the holding of ordinary shares, or all of the circumstances in which holders of ordinary shares may benefit from an exemption or relief from U.K. taxation. It is written on the basis that the company is and remains solely resident in the United Kingdom for tax purposes and will therefore be subject to the U.K. tax regime and not the U.S. tax regime save as set out above under “Material U.S. Federal Income Tax Considerations for U.S. Holders.”

Except to the extent that the position of non-U.K. resident persons is expressly referred to, this guide relates only to persons who are resident for tax purposes solely in the United Kingdom and do not have a permanent establishment or fixed base in any other jurisdiction with which the holding of the ordinary shares is connected, or U.K. Holders, who are absolute beneficial owners of the ordinary shares (and do not hold the ordinary shares through an Individual Savings Account or a Self-Invested Personal Pension) and any dividends paid in respect of the ordinary shares (where the dividends are regarded for U.K. tax purposes as that person's own income).

This guide may not relate to certain classes of U.K. Holders, such as (but not limited to):

- persons who are connected with the company;
- financial institutions;
- insurance companies;
- charities or tax-exempt organizations;
- collective investment schemes;
- pension schemes;
- brokers or dealers in securities or persons who hold ordinary shares otherwise than as an investment;
- persons who have (or are deemed to have) acquired their ordinary shares by virtue of an office or employment or who are or have been officers or employees of the company or any of its affiliates; and
- individuals who are subject to U.K. taxation on a remittance basis.

 THESE PARAGRAPHS ARE A SUMMARY OF CERTAIN U.K. TAX CONSIDERATIONS AND ARE INTENDED AS A GENERAL GUIDE ONLY. IT IS RECOMMENDED THAT ALL HOLDERS OF ORDINARY SHARES OBTAIN ADVICE AS TO THE CONSEQUENCES OF THE ACQUISITION, OWNERSHIP AND DISPOSAL OF THE ORDINARY SHARES IN THEIR OWN PARTICULAR CIRCUMSTANCES FROM THEIR OWN TAX ADVISORS. IN PARTICULAR, NON-U.K. RESIDENTS OR DOMICILED PERSONS ARE ADVISED TO CONSIDER THE POTENTIAL IMPACT OF ANY RELEVANT DOUBLE TAXATION AGREEMENTS.
Dividends

Withholding Tax

Dividends paid by the company will not be subject to any withholding or deduction for or on account of U.K. tax.

Income Tax

An individual U.K. Holder may, depending on his or her particular circumstances, be subject to U.K. tax on dividends received from the company. An individual holder of ordinary shares who is not resident for tax purposes in the United Kingdom should not be chargeable to U.K. income tax on dividends received from the company unless he or she carries on (whether solely or in partnership) a trade, profession or vocation in the United Kingdom through a permanent establishment to which the ordinary shares are attributable.

Dividend income is treated as the top slice of the total income chargeable to U.K. income tax. An individual U.K. Holder who receives a dividend in the 2017/2018 tax year will be entitled to a tax-free allowance of £5,000 (which will reduce to £2,000 for dividends received on or after April 6, 2018). Dividend income in excess of this tax-free allowance will be charged at the highest marginal rate of 7.5% for basic rate taxpayers, 32.5% for higher rate taxpayers, and 38.1% for additional rate taxpayers.

Corporation Tax

A corporate holder of ordinary shares who is not resident for tax purposes in the United Kingdom should not be chargeable to U.K. corporation tax on dividends received from the company unless it carries on (whether solely or in partnership) a trade in the United Kingdom through a permanent establishment to which the ordinary shares are attributable.

Corporate U.K. Holders should not be subject to U.K. corporation tax on any dividend received from the company so long as the dividends qualify for exemption, which should be the case, although certain conditions must be met. If the conditions for the exemption are not satisfied, or such U.K. Holder elects for an otherwise exempt dividend to be taxable, U.K. corporation tax will be chargeable on the amount of any dividends (at the main rate of 19% in 2017/18).

Chargeable Gains

A disposal or deemed disposal of ordinary shares by a U.K. Holder may, depending on the U.K. Holder's circumstances and subject to any available exemptions or reliefs (such as the annual exemption), give rise to a chargeable gain or an allowable loss for the purposes of U.K. capital gains tax and corporation tax on chargeable gains.

If an individual U.K. Holder who is subject to U.K. income tax at either the higher or the additional rate is liable to U.K. capital gains tax on the disposal of ordinary shares, the current applicable rate will be 20%. For an individual U.K. Holder who is subject to U.K. income tax at the basic rate and liable to U.K. capital gains tax on such disposal, the current applicable rate would be 10%, save to the extent that any capital gains exceed the unused basic rate tax band. In that case, the rate currently applicable to the excess would be 20%.

If a corporate U.K. Holder becomes liable to U.K. corporation tax on the disposal of ordinary shares, the main rate of U.K. corporation tax (currently 19%) would apply. An indexation allowance may be available to such a holder to give an additional deduction based on the indexation of its base cost in the shares by reference to U.K. retail price inflation over its holding period. An indexation allowance can only reduce a gain on a future disposal, and cannot create a loss. Finance Bill 2017-18 as published on December 1, 2017 will restrict the application of indexation relief to assets acquired prior
to January 1, 2018, and will also change the calculation of the relief for disposals (or deemed disposals) of such assets on or after January 1, 2018 so as to apply
the Retail Price Index for December 2017, regardless of the actual date of disposal.

A holder of ordinary shares which is not resident for tax purposes in the United Kingdom should not normally be liable to U.K. capital gains tax or
corporation tax on chargeable gains on a disposal of ordinary shares unless the person is carrying on (whether solely or in partnership) a trade, profession or
vocation in the United Kingdom through a permanent establishment, branch or agency to which the ordinary shares are attributable. However, an individual
holder of ordinary shares who has ceased to be resident for tax purposes in the United Kingdom for a period of less than five years and who disposes of ordinary
shares during that period may be liable on his or her return to the United Kingdom to U.K. tax on any capital gain realized (subject to any available exemption or
relief).

Stamp Duty and Stamp Duty Reserve Tax

The discussion below relates to the holders of our ordinary shares wherever resident.

Issue of Ordinary Shares

No U.K. stamp duty or stamp duty reserve tax, or SDRT, is payable on the issue of the underlying ordinary shares in the company.

Transfers of Ordinary Shares

An unconditional agreement to transfer ordinary shares will normally give rise to a charge to SDRT at the rate of 0.5% of the amount or value of the
consideration payable for the transfer. The purchaser of the shares is liable for the SDRT. Transfers of ordinary shares in certificated form are generally also
subject to stamp duty at the rate of 0.5% of the amount or value of the consideration given for the transfer (rounded up to the next £5.00). Stamp duty is normally
paid by the purchaser. The charge to SDRT will be canceled or, if already paid, repaid (generally with interest), where a transfer instrument has been duly stamped
within six years of the charge arising.

An unconditional agreement to transfer ordinary shares to, or to a nominee or agent for, a person whose business is or includes the issue of depositary
receipts or the provision of clearance services will generally be subject to SDRT (and, where the transfer is effected by a written instrument, stamp duty) at a
higher rate of 1.5% of the amount or value of the consideration given for the transfer unless the clearance service has made and maintained an election under
Section 97A of the UK Finance Act 1986, or Finance Act. It is understood that HMRC regards the facilities of DTC as a clearance service for these purposes. We
are not aware of any election by DTC under Section 97A of the Finance Act that would affect our shares issued to Cede.

Based on current published HMRC practice following recent case law, no SDRT is generally payable where the transfer of ordinary shares to a clearance
service or depositary receipt system is an integral part of an issue of share capital. It was announced on November 22, 2017 that the government will not seek to
reintroduce this charge following the departure of the United Kingdom from the European Union.

Any stamp duty or SDRT payable on a transfer of ordinary shares to a depositary receipt system or clearance service will in practice generally be paid by the
participants in the clearance service or depositary receipt system.
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 Leerink Partners LLC are acting as representatives, the following respective numbers of ordinary shares:

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<tr>
<th>Underwriter</th>
<th>Number of Ordinary Shares</th>
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<tbody>
<tr>
<td>Credit Suisse Securities (USA) LLC</td>
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<tr>
<td>Leerink Partners LLC</td>
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<td>SunTrust Robinson Humphrey, Inc.</td>
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<td>Wedbush Securities Inc.</td>
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</tr>
<tr>
<td>Total</td>
<td></td>
</tr>
</tbody>
</table>

The underwriting agreement provides that the underwriters are obligated to purchase all the ordinary shares 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.

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 additional ordinary shares at the initial public offering price less the underwriting discounts and commissions. The option may be exercised only to cover any over-allotments of ordinary shares.

The underwriters propose to offer the ordinary shares 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 ordinary 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:

<table>
<thead>
<tr>
<th>Per Ordinary Share</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without</td>
</tr>
<tr>
<td>Underwriting discounts and commissions paid by us</td>
<td>$</td>
</tr>
<tr>
<td>Expenses payable by us</td>
<td>$</td>
</tr>
</tbody>
</table>

We have also agreed to reimburse the underwriters in an amount up to 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 of our ordinary shares, or securities convertible into or exchangeable or exercisable for any of our ordinary shares, 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 ordinary shares and securities exercisable for or convertible into our ordinary shares outstanding immediately prior to this offering

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have agreed, subject to certain exceptions, that they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any of our ordinary shares, or securities convertible into or exchangeable or exercisable for any of our ordinary shares, 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 ordinary shares, whether any of these transactions are to be settled by delivery of our ordinary shares 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 intend to apply to list our ordinary shares on The Nasdaq Global Market.

Prior to this offering, there has been no public market for our ordinary shares. 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 ordinary 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 the ordinary shares will trade in the public market subsequent to this offering or that an active trading market for the ordinary shares 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 ordinary 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 the ordinary shares 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 ordinary shares 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 ordinary
shares or preventing or retarding a decline in the market price of the ordinary shares. As a result, the price of our ordinary shares 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

The ordinary shares 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

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Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the ordinary 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 ordinary 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 ordinary 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 ordinary 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 ordinary shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of ordinary 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 ordinary shares.

**China**

This prospectus does not constitute a public offer of the ordinary shares offered by this prospectus, whether by sale or subscription, in China. The ordinary 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 ordinary 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 ordinary 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 ordinary 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 ordinary 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 ordinary shares may not be circulated or distributed, nor may the ordinary 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 ordinary 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, ordinary shares, debentures and units of ordinary 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 ordinary 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.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.
LEGAL MATTERS

The validity of the ordinary shares being offered by this prospectus and certain other matters of English law and U.S. federal law will be passed upon for us by Cooley LLP. Certain legal matters related to this offering will be passed upon for the underwriters by Wilmer Cutler Pickering Hale and Dorr LLP.

EXPERTS

The consolidated financial statements of Entasis Therapeutics Limited as of December 31, 2016, and for the year 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.

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

We are incorporated and have our registered office in, and are currently existing under the laws of, England and Wales. In addition, while our officers all currently reside in and most of our tangible assets are located inside the United States, certain of our directors reside and some of our assets are held outside of the United States. As a result, it may not be possible to serve process within the United States on certain directors or us or to enforce judgments obtained in U.S. courts against such directors or us based on civil liability provisions of the securities laws of the United States. As a result, it may not be possible for investors to effect service of process within the United States upon such persons or to enforce judgments obtained in U.S. courts against them or us, including judgments predicated upon the civil liability provisions of the U.S. federal securities laws. In addition, uncertainty exists as to whether the courts of England and Wales would:

- recognize or enforce judgments of United States courts obtained against us or our directors or officers predicated upon the civil liabilities provisions of the securities laws of the United States or any state in the United States; or
- entertain original actions brought in England and Wales against us or our directors or officers predicated upon the securities laws of the United States or any state in the United States.

We have been advised by Cooley LLP that there is currently no treaty between (i) the United States and (ii) England and Wales providing for reciprocal recognition and enforcement of judgments of United States courts in civil and commercial matters (although the United States and the United Kingdom are both parties to the New York Convention on the Recognition and Enforcement of Foreign Arbitral Awards) and that a final judgment for the payment of money rendered by any general or state court in the United States based on civil liability, whether predicated solely upon the United States securities laws, would not be automatically enforceable in England and Wales. We have also been advised by Cooley LLP that any final and conclusive monetary judgment for a definite sum obtained against us in United States courts would be treated by the courts of England and Wales as a cause of action in itself and sued upon as a debt at common law so that no retrial of the issues would be necessary, provided that:

- the relevant U.S. court had jurisdiction over the original proceedings according to English conflicts of laws principles at the time when proceedings were initiated;
- England and Wales courts had jurisdiction over the matter on enforcement and we either submitted to such jurisdiction or were resident or carrying on business within such jurisdiction and were duly served with process;
- the U.S. judgment was final and conclusive on the merits in the sense of being final and unalterable in the court that pronounced it and being for a definite sum of money;
the judgment given by the courts was not in respect of penalties, taxes, fines or similar fiscal or revenue obligations (or otherwise based on a U.S. law that an English court considers to relate to a penal, revenue or other public law);

- the judgment was not procured by fraud;
- recognition or enforcement of the judgment in England and Wales would not be contrary to public policy or the Human Rights Act 1998;
- the proceedings pursuant to which judgment was obtained were not contrary to natural justice;
- the U.S. judgment was not arrived at by doubling, trebling or otherwise multiplying a sum assessed as compensation for the loss or damages sustained and not being otherwise in breach of Section 5 of the U.K. Protection of Trading Interests Act 1980, or is a judgment based on measures designated by the Secretary of State under Section 1 of that Act;
- there is not a prior decision of an English court or the court of another jurisdiction on the issues in question between the same parties; and
- the English enforcement proceedings were commenced within the limitation period.

Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the United States securities laws, including whether the award of monetary damages under such laws would constitute a penalty, is an issue for the court making such decision.

Subject to the foregoing, investors may be able to enforce in England and Wales judgments in civil and commercial matters that have been obtained from U.S. federal or state courts. Nevertheless, we cannot assure you that those judgments will be recognized or enforceable in England and Wales.

If an English court gives judgment for the sum payable under a U.S. judgment, the English judgment will be enforceable by methods generally available for this purpose. These methods generally permit the English court discretion to prescribe the manner of enforcement. In addition, it may not be possible to obtain an English judgment or to enforce that judgment if the judgment debtor is or becomes subject to any insolvency or similar proceedings, or if the judgment debtor has any set-off or counterclaim against the judgment creditor. Also note that, in any enforcement proceedings, the judgment debtor may raise any counterclaim that could have been brought if the action had been originally brought in England unless the subject of the counterclaim was in issue and denied in the U.S. proceedings.

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 ordinary shares 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 ordinary 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 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
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

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Consolidated Balance Sheet  F-3
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Consolidated Statement of Cash Flows  F-6
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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors
Entasis Therapeutics Limited:

We have audited the accompanying consolidated balance sheet of Entasis Therapeutics Limited and subsidiary (the Company) as of December 31, 2016, and the related consolidated statements of operations, redeemable convertible preference shares and shareholder's deficit, and cash flows for the year then ended. 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 audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States) and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Entasis Therapeutics Limited and subsidiary as of December 31, 2016, and the results of their operations and their cash flows for the year then ended in conformity with U.S. generally accepted accounting principles.

/s/ KPMG LLP

Cambridge, Massachusetts
December 8, 2017
## ENTASIS THERAPEUTICS LIMITED

### CONSOLIDATED BALANCE SHEET

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

<table>
<thead>
<tr>
<th>Assets</th>
<th>December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current assets:</td>
<td></td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>$26,256</td>
</tr>
<tr>
<td>Due from related party</td>
<td>234</td>
</tr>
<tr>
<td>Prepaid expenses and other current assets</td>
<td>152</td>
</tr>
<tr>
<td><strong>Total current assets</strong></td>
<td>26,642</td>
</tr>
<tr>
<td>Property and equipment, net</td>
<td>364</td>
</tr>
<tr>
<td>Other assets</td>
<td>63</td>
</tr>
<tr>
<td><strong>Total assets</strong></td>
<td>$27,069</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Liabilities, Redeemable Convertible Preference Shares and Shareholder’s Deficit</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Current liabilities:</td>
<td></td>
</tr>
<tr>
<td>Accounts payable</td>
<td>$898</td>
</tr>
<tr>
<td>Due to related party</td>
<td>620</td>
</tr>
<tr>
<td>Accrued expenses</td>
<td>3,444</td>
</tr>
<tr>
<td><strong>Total current liabilities</strong></td>
<td>4,962</td>
</tr>
<tr>
<td>Deferred rent</td>
<td>34</td>
</tr>
<tr>
<td><strong>Total liabilities</strong></td>
<td>4,996</td>
</tr>
</tbody>
</table>

Commitments (Note 10)

A redeemable convertible preference shares, nominal value of $1.00 per share; 33,499,900 shares issued and outstanding as of December 31, 2016; liquidation and redemption value of $35,699 as of December 31, 2016

B redeemable convertible preference shares, nominal value of $1.00 per share; 25,000,000 shares issued and outstanding as of December 31, 2016; liquidation and redemption value of $25,759 as of December 31, 2016

<table>
<thead>
<tr>
<th>Shareholder's deficit:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ordinary shares, nominal value of $0.20 per share; 100 shares issued and outstanding as of December 31, 2016</td>
<td>---</td>
</tr>
<tr>
<td>Additional paid-in capital</td>
<td>904</td>
</tr>
<tr>
<td>Accumulated deficit</td>
<td>(27,247)</td>
</tr>
<tr>
<td><strong>Total shareholder's deficit</strong></td>
<td>(26,345)</td>
</tr>
<tr>
<td><strong>Total liabilities, redeemable convertible preference shares and shareholder's deficit</strong></td>
<td>$27,069</td>
</tr>
</tbody>
</table>

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

F-3
## CONSOLIDATED STATEMENT OF OPERATIONS

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

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating expenses:</td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>$ 15,778</td>
</tr>
<tr>
<td>General and administrative</td>
<td>3,326</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>19,104</td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(19,104)</td>
</tr>
<tr>
<td>Other income:</td>
<td></td>
</tr>
<tr>
<td>Interest income</td>
<td>9</td>
</tr>
<tr>
<td>Total other income</td>
<td>9</td>
</tr>
<tr>
<td>Net loss</td>
<td>$ (19,095)</td>
</tr>
<tr>
<td>Net loss per share—basic and diluted</td>
<td>$ (190,950.00)</td>
</tr>
<tr>
<td>Weighted average ordinary shares outstanding—basic and diluted</td>
<td>100</td>
</tr>
</tbody>
</table>

The accompanying notes are an integral part of these consolidated financial statements.
## Entasis Therapeutics Limited

**Consolidated Statement of Redeemable Convertible Preference Shares and Shareholder’s Deficit**

(Amounts in thousands, except share amounts)

<table>
<thead>
<tr>
<th></th>
<th>Redeemable Convertible Preference Shares</th>
<th>Ordinary Shares</th>
<th>Additional Paid-in Capital</th>
<th>Accumulated Deficit</th>
<th>Total Shareholder’s Deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Shares</td>
<td>Amount</td>
<td>Shares</td>
<td>Amount</td>
<td>Shares</td>
</tr>
<tr>
<td><strong>Balances as of December 31, 2015</strong></td>
<td>33,499,900</td>
<td>$23,866</td>
<td>—</td>
<td>$—</td>
<td>100</td>
</tr>
<tr>
<td><strong>Issuance of B redeemable convertible preference shares, net of issuance costs of $450</strong></td>
<td>25,000,000</td>
<td>$24,550</td>
<td>—</td>
<td>$—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Share-based compensation expense</strong></td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Net loss</strong></td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Balances as of December 31, 2016</strong></td>
<td>33,499,900</td>
<td>$23,866</td>
<td>25,000,000</td>
<td>$24,550</td>
<td>100</td>
</tr>
</tbody>
</table>

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

F-5
# ENTASIS THERAPEUTICS LIMITED
## CONSOLIDATED STATEMENT OF CASH FLOWS

(Amounts in thousands)

<table>
<thead>
<tr>
<th>Cash flows from operating activities:</th>
<th>Year Ended December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net loss</td>
<td>$ (19,095)</td>
</tr>
<tr>
<td>Adjustments to reconcile net loss to net cash used in operating activities:</td>
<td></td>
</tr>
<tr>
<td>Depreciation and amortization expense</td>
<td>177</td>
</tr>
<tr>
<td>Share-based compensation expense</td>
<td>570</td>
</tr>
<tr>
<td>Changes in operating assets and liabilities:</td>
<td></td>
</tr>
<tr>
<td>Prepaid expenses and other assets</td>
<td>(170)</td>
</tr>
<tr>
<td>Accounts payable</td>
<td>641</td>
</tr>
<tr>
<td>Accrued expenses</td>
<td>1,907</td>
</tr>
<tr>
<td>Deferred rent</td>
<td>17</td>
</tr>
<tr>
<td>Net cash used in operating activities</td>
<td>(15,953)</td>
</tr>
</tbody>
</table>

| Cash flows from investing activities: | | |
| Purchases of property and equipment | (140)                       |
| Net cash used in investing activities| (140)                       |

| Cash flows from financing activities: | | |
| Proceeds from issuance of redeemable convertible preference shares, net of issuance costs | 42,192                     |
| Net cash provided by financing activities | 42,192                     |

| Net increase in cash and cash equivalents | | |
| Cash and cash equivalents at beginning of period | 157                       |
| Cash and cash equivalents at end of period | $ 26,256                   |

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

F-6
1. Organization and Description of Business

Entasis Therapeutics Limited, ("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 ("AZ"). In connection with the spin-out of the Company from AZ in May 2015, the Company issued 100 ordinary shares to AZ. Additionally, pursuant to a business transfer and subscription agreement with AZ, the Company also issued 33,499,900 A redeemable convertible preference shares ("A Preference Shares") to AZ 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 AZ 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.

Liquidity

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 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 a net loss of $19.1 million for the year ended December 31, 2016. In addition, as of December 31, 2016, the Company had an accumulated deficit of $27.2 million. The Company expects to continue to generate operating losses for the foreseeable future.

As of December 8, 2017, the issuance date of these consolidated financial statements, the Company expects its cash and cash equivalents of $26.3 million as of December 31, 2016, together with the $56.3 million of net cash proceeds from the Company's sale of B-1 redeemable convertible preference shares ("B-1 Preference Shares") will be sufficient to fund its operating expenses and capital expenditure requirements through March 2019.

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 Company expects to seek additional funding through equity financings, debt financings or other capital
1. Organization and Description of Business (Continued)

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.

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.

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, the carrying amount of cash equivalents was $19.7 million, 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.
2. Summary of Significant Accounting Policies (Continued)

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 shareholder's 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 did not record any deferred offering costs as of December 31, 2016.

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:

<table>
<thead>
<tr>
<th>Asset Type</th>
<th>Estimated Useful Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory equipment</td>
<td>3 - 5 years</td>
</tr>
<tr>
<td>Computer software</td>
<td>3 years</td>
</tr>
</tbody>
</table>

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
2. Summary of Significant Accounting Policies (Continued)

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

**Government Contracts and Grant Agreements**

Income from grants is recognized in the period during which the related qualifying 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,
2. Summary of Significant Accounting Policies (Continued)

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

The Company has entered into various research and development contracts with research institutions and other companies. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

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

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 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, 2016 under ASC 740-10.

**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, the outstanding A Preference Shares and B Preference Shares have been excluded from the calculation because their effects would be antidilutive. Therefore, the weighted-average shares used to calculate both basic and diluted loss per share are the same. The following potentially dilutive securities have been excluded from the computation of diluted weighted-average shares outstanding as they would be antidilutive:

<table>
<thead>
<tr>
<th>Securities</th>
<th>Year Ended December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Options to purchase ordinary shares</td>
<td>8,314,836</td>
</tr>
<tr>
<td>Redeemable convertible preference shares (as converted into ordinary shares)</td>
<td>58,499,900</td>
</tr>
<tr>
<td></td>
<td>66,814,736</td>
</tr>
</tbody>
</table>
2. Summary of Significant Accounting Policies (Continued)

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 update explicitly require a company's management to assess an entity's ability to continue 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 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 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.
2. Summary of Significant Accounting Policies (Continued)

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.

3. Property and Equipment, Net

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

<table>
<thead>
<tr>
<th>Description</th>
<th>December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory equipment</td>
<td>$ 575</td>
</tr>
<tr>
<td>Computer software</td>
<td>63</td>
</tr>
<tr>
<td>Total</td>
<td>638</td>
</tr>
<tr>
<td>Less: Accumulated depreciation</td>
<td>(274)</td>
</tr>
<tr>
<td>Property and equipment, net</td>
<td>$ 364</td>
</tr>
</tbody>
</table>

Depreciation expense for the year ended December 31, 2016 was $0.2 million.

4. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

<table>
<thead>
<tr>
<th>Description</th>
<th>December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accrued compensation and benefits</td>
<td>$ 1,073</td>
</tr>
<tr>
<td>Accrued contract manufacturing</td>
<td>1,789</td>
</tr>
<tr>
<td>Accrued clinical trial costs</td>
<td>302</td>
</tr>
<tr>
<td>Accrued professional services</td>
<td>140</td>
</tr>
<tr>
<td>Other</td>
<td>140</td>
</tr>
<tr>
<td>Total accrued expenses</td>
<td>$ 3,444</td>
</tr>
</tbody>
</table>

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 qualified 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 qualified research expenditures incurred and paid by the Company during the performance period.
5. Funding Arrangements (Continued)

As of December 31, 2016, no funding had been received and no qualified expenses had been incurred under the USAMRAA grant. Accordingly, no grant income has been recognized for the year ended December 31, 2016.

6. Redeemable Convertible Preference Shares

As of December 31, 2016, the redeemable convertible preference shares consisted of the following (in thousands, except share amounts):

<table>
<thead>
<tr>
<th>preference shares</th>
<th>Issued and Outstanding</th>
<th>Carrying Value</th>
<th>Liquidation and Redemption Value</th>
<th>Ordinary Shares Issuable Upon Conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>A preference shares</td>
<td>33,499,900</td>
<td>$23,866</td>
<td>$35,699</td>
<td>33,499,900</td>
</tr>
<tr>
<td>B preference shares</td>
<td>25,000,000</td>
<td>24,550</td>
<td>25,759</td>
<td>25,000,000</td>
</tr>
<tr>
<td>Total</td>
<td>58,499,900</td>
<td>$48,416</td>
<td>$61,458</td>
<td>58,499,900</td>
</tr>
</tbody>
</table>

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 $110.0 million. 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, 2016, the Company is authorized to subscribe for, or convert securities into, shares of the Company, up to a remaining nominal value of $49.8 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 shareholder’s 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 AZ 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 AZ in consideration for property and equipment, clinical materials, intellectual property and net cash proceeds of $23.3 million, of which $17.6 million of the cash proceeds were received during 2016.

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. 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. See Note 13.
6. Redeemable Convertible Preference Shares (Continued)

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 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 and B Preference Shares were $2.2 million and $0.8 million as of December 31, 2016, respectively, although no dividends have been declared by the Company's board of directors. Management has determined that it is not probable the Company will pay dividends, whether by the board of directors' declaration or a liquidation event, and therefore has not accrued any dividends payable as of December 31, 2016.

**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).
6. Redeemable Convertible Preference Shares (Continued)

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 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 AZ; 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-one 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, 2016, no cash dividends have been declared or paid.

In May 2015, in conjunction with the spin-out of the Company, the Company issued 100 ordinary shares to AZ. As of December 31, 2016, the ordinary shares have a nominal value of $0.20 per share and there were 100 ordinary shares issued and outstanding.
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. As of December 31, 2016, the 2015 Plan allows for a maximum of 14,735,294 ordinary shares to be issued and there were 6,420,458 ordinary shares available for grant.

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 year ended December 31, 2016, the Company granted options to purchase 3,752,683 ordinary shares to employees and directors. The Company recorded share-based compensation expense for options granted to employees and directors of $0.2 million during the year ended December 31, 2016.

During the year ended December 31, 2016, the Company granted options to purchase 175,032 ordinary shares to non-employees. The Company recorded share-based compensation expense for options granted to non-employees of $10,000 during the year ended December 31, 2016.

The following table summarizes the Company’s option activity under the 2015 Plan:

<table>
<thead>
<tr>
<th></th>
<th>Number of Shares</th>
<th>Weighted Average Exercise Price</th>
<th>Weighted Average Remaining Contractual Term (Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outstanding at December 31, 2015</td>
<td>4,702,415</td>
<td>$0.24</td>
<td>9.63</td>
</tr>
<tr>
<td>Granted</td>
<td>3,927,715</td>
<td>$0.18</td>
<td></td>
</tr>
<tr>
<td>Forfeited</td>
<td>(315,294)</td>
<td>$0.24</td>
<td></td>
</tr>
<tr>
<td>Outstanding at December 31, 2016</td>
<td>8,314,836</td>
<td>$0.21</td>
<td>9.19</td>
</tr>
<tr>
<td>Options exercisable as of December 31, 2016</td>
<td>1,920,959</td>
<td>$0.24</td>
<td>8.71</td>
</tr>
<tr>
<td>Options unvested as of December 31, 2016</td>
<td>6,393,877</td>
<td>$0.20</td>
<td>9.33</td>
</tr>
</tbody>
</table>

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. As of December 31, 2016, there was no intrinsic value associated with the options.

The weighted average grant-date fair value per share of share options granted during the year ended December 31, 2016 was $0.10 per share. The total fair value of options vested during the year ended December 31, 2016 was $0.2 million.
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:

| Weighted average risk-free interest rate | 1.39% |
| Expected term (in years) | 6.10 |
| Expected volatility | 60.50% |
| Expected dividend yield | 0.00% |

The fair value of ordinary shares used to determine the grant-date fair value for all options granted during the year ended December 31, 2016 was $0.18.

**AZ Shares Option and Incentive Plan**

Certain employees of the Company participate in the AZ Shares Option and Incentive Plan (the "AZ Plan"), whereby employees of the Company continue to vest in the restricted shares ("AZ RSUs") of AZ ordinary shares issued by AZ to the employees prior to employment by the Company. AZ RSUs vest 100% after 36 months and will be fully vested in March 2017.

The Company recorded share-based compensation expense for AZ RSUs of $0.4 million during the year ended December 31, 2016, included in the table presented below. The Company’s compensation expense related to the AZ RSUs is based on the fair value of AZ’s ordinary shares as of the date of the issuance to the employees during their employment at AZ. 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 AZ no longer held a controlling interest in the Company, the Company became an equity method investment of AZ. 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 AZ.

**Share-Based Compensation**

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

<table>
<thead>
<tr>
<th>Year Ended December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research and development</td>
</tr>
<tr>
<td>General and administrative</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

As of December 31, 2016, total unrecognized compensation expense related to the unvested options was $0.7 million, which is expected to be recognized over the weighted average period of approximately 3.0 years. As of December 31, 2016, total unrecognized compensation expense related to
8. Share-Based Compensation (Continued)

The unvested AZ RSUs was $0.1 million, all of which is expected to be recognized during the first quarter of 2017.

9. Income Taxes

During the year ended December 31, 2016, the Company recorded no income tax benefit 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 year ended December 31, 2016 consisted of the following (in thousands):

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>$13,410</td>
</tr>
<tr>
<td>United States</td>
<td>5,685</td>
</tr>
<tr>
<td></td>
<td><strong>$19,095</strong></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Income tax benefit computed at U.K. statutory tax rate</td>
<td>20.0%</td>
</tr>
<tr>
<td>State taxes, net of federal benefit</td>
<td>1.3</td>
</tr>
<tr>
<td>Foreign rate differential</td>
<td>4.2</td>
</tr>
<tr>
<td>Research and development tax credits</td>
<td>3.0</td>
</tr>
<tr>
<td>Permanent difference</td>
<td>(1.0)</td>
</tr>
<tr>
<td>Valuation allowances</td>
<td>(27.5)</td>
</tr>
<tr>
<td>Effective income tax rate</td>
<td><strong>0.0%</strong></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deferred tax assets:</td>
<td></td>
</tr>
<tr>
<td>Net operating loss carryforwards</td>
<td>$4,924</td>
</tr>
<tr>
<td>Tax credit carryforwards</td>
<td>806</td>
</tr>
<tr>
<td>Accrued expenses and other</td>
<td>689</td>
</tr>
<tr>
<td>Total deferred tax assets</td>
<td><strong>6,419</strong></td>
</tr>
<tr>
<td>Depreciation and amortization</td>
<td>(4)</td>
</tr>
<tr>
<td>Total deferred tax liabilities</td>
<td><strong>(4)</strong></td>
</tr>
<tr>
<td>Valuation allowance</td>
<td>(6,415)</td>
</tr>
<tr>
<td>Net deferred tax assets</td>
<td><strong>$—</strong></td>
</tr>
</tbody>
</table>
9. Income Taxes (Continued)

As of December 31, 2016, the Company had U.S. federal and state net operating loss carryforwards ("NOLs") of $5.7 million and $5.5 million, respectively, which begin to expire in 2035. As of December 31, 2016, the Company had federal and state research and development tax credits carryforwards of $0.6 million and $0.3 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, 2016, the Company had NOLs in the United Kingdom of $13.4 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 $6.4 million has been established against the deferred tax assets as of December 31, 2016.

Changes in the valuation allowance for deferred tax assets during the year ended December 31, 2016 related primarily to the increases in NOLs and research and development tax credit carryforwards and were as follows (in thousands):

<table>
<thead>
<tr>
<th>Description</th>
<th>Year Ended December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valuation allowance at beginning of year</td>
<td>$ (1,183)</td>
</tr>
<tr>
<td>Increases recorded to income tax provision</td>
<td>(5,232)</td>
</tr>
<tr>
<td>Valuation allowance at end of year</td>
<td>$ (6,415)</td>
</tr>
</tbody>
</table>

The Company has not recorded an amount for unrecognized tax benefits or related interest and penalties accrued as of December 31, 2016. 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.
9. Income Taxes (Continued)

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. Commitments

Lease Commitments

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

Future minimum lease payments as of December 31, 2016 were as follows (in thousands):

<table>
<thead>
<tr>
<th>Year Ending December 31</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>$376</td>
</tr>
<tr>
<td>2018</td>
<td>389</td>
</tr>
<tr>
<td>2019</td>
<td>402</td>
</tr>
<tr>
<td>2020</td>
<td>146</td>
</tr>
<tr>
<td></td>
<td>$1,313</td>
</tr>
</tbody>
</table>

A Subscription Agreement

In connection with the A Subscription Agreement, the Company agreed to pay AZ 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 AZ 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 AZ tiered,
single-digit, per-country royalties on the annual worldwide net sales of ETX2514 and zoliflodacin.

11. Related Party Transactions

The Company was formed in May 2015 as a wholly owned subsidiary of AZ, which maintained a controlling interest in the Company until the B Preference
Shares were issued in March 2016. As of December 31, 2016, AZ was the sole ordinary shareholder and the sole A Preference Shareholder.

Subscription Receivable Due from AZ

In connection with the issuance and sale of A Preference Shares, AZ 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 AZ, as property of the Company. This
11. Related Party Transactions (Continued)

arrangement ceased upon the closing the B Preference 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 AZ. See Note 10.

Share-Based Compensation

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

AZ Transition Services Agreement

The Company and AZ 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, with such amount included in due to related party on the consolidated balance sheet.

12. 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 in 2016.

13. Subsequent Events

The Company evaluated subsequent events through December 8, 2017, the date on which these consolidated financial statements were issued.

Funding Agreements

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 approximately $16.4 million of qualified research expenditures of the Company from April 2017 through September 2021.

Issuance of Share-Based Options

In November 2017, the Company granted options to purchase 8,090,279 ordinary shares to employees and directors and options to purchase 60,563 ordinary shares to non-employees.

Sales of B-1 Redeemable Convertible Preference Shares

On August 25, 2017, the Company entered into an Entasis Therapeutics Limited B-1 Preference Share Subscription Agreement (the "B-1 Subscription Agreement") and the Amended and Restated
13. Subsequent Events (Continued)

Shareholders' Agreement Relating to Entasis Therapeutics Limited (the "B-1 Shareholders' Agreement"). 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 gross proceeds of $25.0 million (net proceeds of $24.4 million).

Pursuant to the B-1 Subscription Agreement, upon an issuance trigger event ("ITE"), the Company shall sell and issue an additional 54,067,796 B-1 Preference Shares at $0.59 per share, allocated among the investors in the same proportions as the initial B-1 Preference Shares purchases. The ITE may be accelerated by written notice signed by the majority of the board of directors and holders of B-1 Preference Shares. On December 6, 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 gross and net proceeds of $31.9 million. Upon the closing of the second tranche of B-1 Preference Shares, the Company has received gross proceeds of $56.9 million from the sale of B-1 Preference Shares.
PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth all costs and expenses, other than underwriting discounts and commissions, payable by us in connection with the sale of the ordinary shares being registered. All amounts shown are estimates except for the SEC registration fee, the Financial Industry Regulatory Authority, or FINRA, filing fee and The Nasdaq Global Market initial listing fee.

<table>
<thead>
<tr>
<th>Amount to be Paid</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$</td>
<td>SEC registration fee</td>
</tr>
<tr>
<td>$</td>
<td>FINRA filing fee</td>
</tr>
<tr>
<td>$</td>
<td>The Nasdaq Global Market initial listing fee</td>
</tr>
<tr>
<td>$</td>
<td>Printing and engraving expenses</td>
</tr>
<tr>
<td>$</td>
<td>Legal fees and expenses</td>
</tr>
<tr>
<td>$</td>
<td>Accounting fees and expenses</td>
</tr>
<tr>
<td>$</td>
<td>Transfer agent and registrar fees and expenses</td>
</tr>
<tr>
<td>$</td>
<td>Miscellaneous fees and expenses</td>
</tr>
<tr>
<td>$</td>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>

* To be filed by amendment.


Our articles of association provide that, subject to the Companies Act 2006, we shall indemnify, out of our assets, any director of ours or any associated company against all losses, liabilities and expenditures which he or she may sustain or incur in the execution of the duties of his or her office or otherwise in relation thereto.

The relevant provisions under the Companies Act 2006 are Sections 205, 206, 232, 233, 234, 235, 236, 237, 238 and 1157.

Section 205 provides that shareholder approval is not required for a company to provide a director with the funds to meet expenditures incurred or to be incurred in defending any criminal or civil proceedings or in connection with any alleged negligence, default, breach of duty or breach of trust by him in relation to the company or an associated company or any application under sections 661(3) and 661(4) (acquisition of shares by innocent nominee) or section 1157 (described below). Such financial assistance must be repaid if the director is convicted, judgment is found against such director or the court refuses to grant the relief on the application.

Section 206 provides that shareholder approval is not required for a company to provide a director with the funds to meet expenditures incurred or to be incurred by him or her in defending in an investigation by a regulatory authority, or against action proposed to be taken by a regulatory authority, in connection with any alleged negligence, default, breach of duty or breach of trust by him or her in relation to the company or an associated company.

Section 232 provides that any provision that purports to exempt a director (to any extent) from liability in connection with any negligence, default, breach of duty or trust by him or her in relation to the company is void. Any provision by which a company directly or indirectly provides an indemnity (to any extent) for a director of the company or an associated company against any such liability is also void unless permitted by section 233, 234 or 235 (each, described below).
Section 233 permits liability insurance, commonly known as directors' and officers' liability insurance, purchased and maintained by a company against liability for negligence, default, breach of duty or breach of trust in relation to the company.

Section 234 provides that provisions indemnifying directors against liability for negligence, default, breach of duty or breach of trust in relation to the company is not void if that indemnity is a qualifying third-party indemnity. An indemnity is a qualifying third party indemnity as long as it does not provide: (i) any indemnity against any liability incurred by the director to the company or to any associated company; (ii) any indemnity against any liability incurred by the director to pay a fine imposed in criminal proceedings or a sum payable to a regulatory authority by way of a penalty in respect of non-compliance with any requirement of a regulatory nature; and (iii) any indemnity against any liability incurred by the director in defending criminal proceedings in which he or she is convicted, civil proceedings brought by the company or an associated company in which judgment is given against such director or where the court refuses to grant such director relief under an application under sections 661(3) and 661(4) (acquisition of shares by innocent nominee) or its power under section 1157 (described below).

Section 235 provides that provisions indemnifying directors against liability for negligence, default, breach of duty or breach of trust in relation to the company is not void if that indemnity is a qualifying pension scheme indemnity provision. An indemnity is a pension scheme indemnity provision if it provides an indemnity to a director if the company that is a trustee of an occupational pension scheme, with such indemnity to protect against liability incurred in connection with the company's activities as trustee of the scheme.

Any indemnity provided under Section 234 or Section 235 in force for the benefit of one or more directors of the company or an associated company must be disclosed in the directors' annual report in accordance with Section 236 and copies of such indemnification provisions made available for inspection in accordance with Section 237 (and every shareholder has a right to inspect and request such copies under Section 238).

Section 1157 provides that in proceedings against an officer of a company for negligence, default, breach of duty or breach of trust, the court may relieve such officer from liability if it appears to the court that such officer may be liable but acted honestly and reasonably and that having regard to all the circumstances of the case, such officer ought fairly to be excused. Further, an officer who has reason to apprehend that a claim of negligence, default, breach of duty or breach of trust will or might be made against him or her, such officer may apply to the court for relief, and the court will have the same power to relieve such officer as it would if the proceedings had actually been brought.

A court has wide discretion in granting relief, and may authorize civil proceedings to be brought in the name of the company by a shareholder on terms that the court directs. Except in these limited circumstances, English law does not generally permit class-action lawsuits by shareholders on behalf of the company or on behalf of other shareholders.

In connection with this offering, we intend to enter into indemnification agreements with each of our directors and executive officers. Pursuant to these agreements, we agree to indemnify these individuals to the fullest extent permissible under English law against liabilities arising out of, or in connection with, the actual or purported exercise of, or failure to exercise, any of his or her powers, duties or responsibilities as a director or officer, and to advance expenses incurred as a result of any proceeding against them as to which they could be indemnified. We also agree to use all reasonable endeavors to provide and maintain appropriate directors' and officers' liability insurance (including ensuring that premiums are properly paid) for their benefit for so long as any claims may lawfully be brought against them.
We have obtained and expect to continue to maintain insurance policies under which our directors and officers are insured, within the limits and subject to the limitations of those policies, against certain expenses in connection with the defense of, and certain liabilities that might be imposed as a result of, actions, suits or proceedings to which they are parties by reason of being or having been directors or officers. The coverage provided by these policies may apply whether or not we would have the power to indemnify such person against such liability under the provisions of English law.

In any underwriting agreement we enter into in connection with the sale of ordinary shares being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, members of our board of directors, members of management and persons who control us within the meaning of the Securities Act, against certain liabilities.

Item 15. Recent Sales of Unregistered Securities.

Issuances of Share Capital

The following list sets forth information regarding all unregistered securities sold by us since March 6, 2015, the date of our inception, through the date of the prospectus that forms a part of this registration statement.

1) In March 2015, we issued 100 ordinary shares to AstraZeneca at a purchase price of $1.00 per ordinary share, for aggregate consideration of $100.

2) In May 2015, we issued 33,499,900 A preference shares to AstraZeneca at a purchase price of $1.00 per share, for aggregate consideration of $33,499,900.

3) In March 2016, we issued an aggregate of 25,000,000 B preference shares to five investors at a purchase price of $1.00 per share, for aggregate consideration of $25,000,000.

4) In August 2017, we issued an aggregate of 42,372,882 B-1 preference shares to eight investors at a purchase price of $0.59 per share, for aggregate consideration of $25,000,000.

5) In December 2017, we issued an aggregate of 54,067,796 B-1 preference shares to eight investors at a purchase price of $0.59 per share, for aggregate consideration of $31,900,000.

The offers, sales and issuances of the securities described in the paragraphs above were exempt from registration under Section 4(a)(2) of the Securities Act and Regulation D promulgated under the Securities Act. The recipients represented to us that they acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions. The recipients also represented to us that they were accredited investors as defined in Rule 501 promulgated under the Securities Act.

Share Option Grants

From March 6, 2015, the date of our inception, through the date of the prospectus that is a part of this registration statement, we have granted options under our 2015 stock incentive plan to purchase an aggregate of 17,884,334 ordinary shares to employees, consultants and directors, having exercise prices ranging from $0.15 to $0.24 per ordinary share. Of these, 261,992 ordinary shares have been issued upon the exercise of share options, at a weighted average exercise price of $0.22 per ordinary share, for aggregate proceeds of $45,450 and 798,012 share options have been cancelled.

The offers, sales and issuances of the securities described in the foregoing paragraph were exempt from registration under Rule 701 promulgated under the Securities Act in that the transactions were under compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of such securities were our employees, directors or consultants and received the
securities under our 2015 stock incentive plan. Appropriate legends were affixed to the securities issued in these transactions.


(a) Exhibits.

<table>
<thead>
<tr>
<th>Exhibit Number</th>
<th>Description of Document</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1†</td>
<td>Form of Underwriting Agreement.</td>
</tr>
<tr>
<td>3.1#</td>
<td>Amended and Restated Articles of Association, as currently in effect.</td>
</tr>
<tr>
<td>3.2†</td>
<td>Form of Amended and Restated Articles of Association, to be in effect upon the closing of this offering.</td>
</tr>
<tr>
<td>4.1†</td>
<td>Form of Specimen stock certificate evidencing ordinary shares.</td>
</tr>
<tr>
<td>4.2†</td>
<td>Registration Rights Agreement, to be in effect upon the closing of this offering.</td>
</tr>
<tr>
<td>5.1†</td>
<td>Opinion of Cooley (UK) LLP as to legality.</td>
</tr>
<tr>
<td>10.3**</td>
<td>Amendment No. 2 to Amended and Restated Business Transfer and Subscription Agreement, dated as of January 2018, by and among AstraZeneca AB, AstraZeneca UK Limited, AstraZeneca Pharmaceuticals LP, Entasis Therapeutics, Inc. and the Registrant.</td>
</tr>
<tr>
<td>10.5+#</td>
<td>Amended and Restated Stock Incentive Plan.</td>
</tr>
<tr>
<td>10.6+#</td>
<td>Form of Nonqualified Stock Option Agreement (Senior Management) under the Amended and Restated Stock Incentive Plan.</td>
</tr>
<tr>
<td>10.7+#</td>
<td>Form of Incentive Stock Option Agreement (Senior Management) under the Amended and Restated Stock Incentive Plan.</td>
</tr>
<tr>
<td>10.8†+</td>
<td>Form of 2018 Equity Incentive Plan.</td>
</tr>
<tr>
<td>10.9†+</td>
<td>Form of Share Option Grant Notice and Share Option Agreement under the 2018 Equity Incentive Plan.</td>
</tr>
<tr>
<td>10.10†+</td>
<td>Form of Restricted Share Unit Grant Notice and Restricted Share Unit Award Agreement under the 2018 Equity Incentive Plan.</td>
</tr>
<tr>
<td>10.11†+</td>
<td>Employment Agreement with Manoussos Perros.</td>
</tr>
<tr>
<td>10.13†+</td>
<td>Employment Agreement with Ruben Tommasi.</td>
</tr>
<tr>
<td>10.14†+</td>
<td>Employment Agreement with Michael Gutch.</td>
</tr>
<tr>
<td>10.15†+</td>
<td>Employment Agreement with Robin Isaacs.</td>
</tr>
<tr>
<td>10.16†+</td>
<td>Form of Indemnification Agreement.</td>
</tr>
</tbody>
</table>
No financial statement schedules have been submitted because they are not required or are not applicable or because the information required is included in the consolidated financial statements or the notes thereto.

Item 17.  Undertakings.

The undersigned Registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this Registration Statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this Registration Statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
SIGNATURES

Pursuant to the requirements of the Securities Act, the Registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Waltham, Commonwealth of Massachusetts, on the day of , 2018.

ENTASIS THERAPEUTICS LIMITED

By: ____________________________________________________________

Manoussos Perros, Ph.D.
President and Chief Executive Officer

KNOWN ALL BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Manoussos Perros, Ph.D., Michael Gutch, Ph.D. and Brent B. Siler, and each of them, his or her true and lawful agent, proxy and attorney-in-fact, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to (i) act on, sign and file with the Securities and Exchange Commission any and all amendments (including post-effective amendments) to this registration statement together with all schedules and exhibits thereto and any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended, together with all schedules and exhibits thereto, (ii) act on, sign and file such certificates, instruments, agreements and other documents as may be necessary or appropriate in connection therewith, (iii) act on and file any supplement to any prospectus included in this registration statement or any such amendment or any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and (iv) take any and all actions which may be necessary or appropriate to be done, as fully for all intents and purposes as he or she might or could do in person, hereby approving, ratifying and confirming all that such agent, proxy and attorney-in-fact or any of his substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<table>
<thead>
<tr>
<th>Signature</th>
<th>Title</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manoussos Perros, Ph.D.</td>
<td>President, Chief Executive Officer (Principal Executive Officer)</td>
<td>2018</td>
</tr>
<tr>
<td>Michael Gutch, Ph.D.</td>
<td>Chief Financial Officer and Chief Business Officer (Principal Financial Officer and Principal Accounting Officer)</td>
<td>2018</td>
</tr>
<tr>
<td>Nicholas Galakatos, Ph.D.</td>
<td>Director</td>
<td>2018</td>
</tr>
<tr>
<td>Heather Behanna, Ph.D.</td>
<td>Director</td>
<td>2018</td>
</tr>
<tr>
<td>Thomas Dyrberg, M.D., D.M.Sc.</td>
<td>Director</td>
<td>2018</td>
</tr>
<tr>
<td>Signature</td>
<td>Title</td>
<td>Date</td>
</tr>
<tr>
<td>--------------------</td>
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</tr>
<tr>
<td>Robert Hopfner, Ph.D.</td>
<td>Director</td>
<td>2018</td>
</tr>
<tr>
<td>Gregory Norden</td>
<td>Director</td>
<td>2018</td>
</tr>
<tr>
<td>Heather Preston, M.D.</td>
<td>Director</td>
<td>2018</td>
</tr>
<tr>
<td>Andrew J. Staples</td>
<td>Director</td>
<td>2018</td>
</tr>
<tr>
<td>James N. Topper, M.D., Ph.D.</td>
<td>Director</td>
<td>2018</td>
</tr>
</tbody>
</table>
SIGNATURE OF AUTHORIZED U.S. REPRESENTATIVE OF THE REGISTRANT

Pursuant to the Securities Act, the undersigned, the duly authorized representative in the United States of Entasis Therapeutics Limited has signed this registration statement or amendment thereto on the day of , 2018.

By:  

______________________________

Manoussos Perros, Ph.D.

President and Chief Executive Officer
AMENDED AND RESTATED
BUSINESS TRANSFER AND
SUBSCRIPTION AGREEMENT

by and among

ASTRAZENECA AB (PUBL),
ASTRAZENECA UK LIMITED,
ASTRAZENECA PHARMACEUTICALS LP
ENTASIS THERAPEUTICS LIMITED

and

ENTASIS THERAPEUTICS INC.

dated as of March 29, 2016

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SECTION 1.02. Definitions
SECTION 1.03. Interpretation and Rules of Construction

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SECTION 2.02. Assumption and Exclusion of Liabilities
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SECTION 2.04. Subscription for Shares
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SECTION 2.08. Closing Deliveries by the Companies

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SECTION 5.04. Business Confidential Information
SECTION 5.05. Publicity
SECTION 5.06. Wrong Pockets
SECTION 5.07. Indemnification
This AMENDED AND RESTATED BUSINESS TRANSFER AND SUBSCRIPTION AGREEMENT (this "Agreement"), dated as of March 5, 2016, is entered into by and among AstraZeneca AB (PUBL), a company incorporated in Sweden under no. 556011-7482 (the "Sweden Seller"), AstraZeneca UK Limited, a company incorporated in England under no. 3674842 (the "UK Seller"), AstraZeneca Pharmaceuticals LP, a Delaware limited partnership (the "US Seller", and together with the Sweden Seller and the UK Seller, the "Sellers"), Entasis Therapeutics Limited, a private limited company incorporated in England and Wales (the "UK Company"), and Entasis Therapeutics Inc., a Delaware corporation and a wholly owned subsidiary of the UK Company (the "US Company", and together with the UK Company, the "Companies").

WHEREAS, the Sellers previously conducted research, discovery and Development activities, including the making of all related regulatory filings in relevant jurisdictions, with respect to the Compounds and the Programs (the "Small Molecule Anti-Infective Program");

WHEREAS, at Closing, the Sellers sold to the Companies, and the Companies purchased from the Sellers, the Transferred Assets, and in connection therewith, the Companies assumed from the Sellers all of the Assumed Liabilities, in each case, upon the terms and subject to the conditions set forth herein;

WHEREAS, at Closing, the Sweden Seller subscribed for, and the UK Company issued to the Sweden Seller, 33,499,900 A Preference Shares for an aggregate subscription price of $33,499,900 in cash;

**ARTICLE VI EMPLOYEE MATTERS**

| SECTION 6.01. | Offer of Employment |
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| SECTION 7.08. | Waiver |
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| SECTION 7.13. | Specific Performance |
| SECTION 7.14. | Counterparts |

**EXHIBITS**

1.01(a) Form of Assignment of Transferred Intellectual Property
1.01(b) Form of Assignment and Assumption Agreement
1.01(c) Description of AZD-0914
1.01(d) Description of AZD-2514
1.01(e) Form of Bill of Sale
2.05(e) Royalties

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
WHEREAS, in accordance with the Shareholders’ Agreement as it was originally executed on Closing and prior to its amendment and restatement on or about the date of this Agreement, upon the terms and subject to the conditions set forth therein, the Sweden Seller committed to subscribe for an additional 16,500,000 A Preference Shares no later than nine (9) months following Closing for an aggregate subscription price of $16,500,000 in cash, which subscription and issuance was to be consummated pursuant to a subscription agreement in the form attached as Schedule 9 to such original Shareholders’ Agreement; and

WHEREAS, in connection with the allotment and issuance of B Preference Shares to the B Preference Subscribers pursuant to the terms of the B Preference Subscription Agreement, the Parties hereto desire to amend and restate the existing business transfer and subscription agreement dated May 11, 2015 entered into between the Parties (the “Original BTSA”) on the terms and conditions set forth herein.

NOW, THEREFORE, in consideration of the promises and the mutual agreements and covenants hereinafter set forth, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, and intending to be legally bound, the Sellers and the Companies hereby agree as follows:

1

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

ARTICLE I
DEFINITIONS

SECTION 1.01. Certain Defined Terms. For purposes of this Agreement:

“A Preference Shares” means the A preference shares of $1.00 each in the capital of the UK Company having the rights that are set out in the Articles of Association and the Shareholders’ Agreement.

“Action” means any claim, action, suit, arbitration, inquiry, proceeding or investigation by or before any Governmental Authority.

“Affiliate” means, with respect to any specified Person, any other Person directly or indirectly controlling or controlled by or under direct or indirect common control with such specified Person. For purposes of this definition, “control” when used with respect to any specified Person means the power to direct the management and policies of such Person, directly or indirectly, whether through the ownership of more than fifty percent (50%) of the outstanding voting securities, by contract or otherwise, and the terms “controlling” and “controlled” have meanings correlative to the foregoing.

“Ancillary Agreements” means the Articles of Association, Assignment of Transferred Intellectual Property, the Assignment and Assumption Agreement, the Bill of Sale, the Employment Agreements, the Lease, the Management Carve-Out Payment Agreement, the Offer Letters, the Shareholders’ Agreement and the Transition Services Agreement.

“Articles of Association” means the articles of association of the UK Company in the form annexed to the Shareholders’ Agreement as Appendix 2, as amended from time to time.

“Assignment of Transferred Intellectual Property” means the Assignment of Transferred Intellectual Property to be executed by the Sellers at the Closing, substantially in the form of Exhibit 1.01(a).

“Assignment and Assumption Agreement” means the Assignment and Assumption Agreement to be executed by the Companies and the Sellers at the Closing, substantially in the form of Exhibit 1.01(b).

“AZD-0914” means [*] as described on Exhibit 1.01(c), or any [*] of the foregoing.

“AZD-0914 Product” means a pharmaceutical product that contains AZD-0914 or [*] of AZD-0914.

“AZD-2514” means a drug that [*] as described on Exhibit 1.01(d), or any [*] of the foregoing.

"AZD-2514 Product" means a pharmaceutical product that contains AZD-2514 or [*] of AZD-2514.

“B Preference Shares” means the B preference shares of $1.00 each in the capital of the UK Company having the rights that are set out in the Articles of Association and the Shareholders’ Agreement.


“B Preference Subscription Agreement” means the subscription agreement between the UK Company and the B Preference Subscribers dated on or about the date of this Agreement in respect of the subscription by such B Preference Subscribers for B Preference Shares in the UK Company.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
“Bill of Sale” means the Bill of Sale to be executed by the Sellers at the Closing, substantially in the form of Exhibit 1.01(e).

“Biological Tools” means (a) laboratory generated bacterial strains and plasmids, (b) biochemistry reagents (including proteins and substrates), (c) molecular and cellular biology reagents and (d) expression plasmids and proteins from TPAT, in each case, exclusively relating to a Legacy Program.

“Business Day” means any day that is not a Saturday, a Sunday or other day on which banks are required or authorized by Law to be closed in New York, New York, the City of London, England, and Södertälje, Sweden.

“Calendar Quarter” means the respective period of three consecutive calendar months ending on March 31, June 30, September 30 and December 31.

“Closing” means the sale and purchase of the Transferred Assets and the subscription by, and issuance to, the Sweden Seller of the UK Company Shares contemplated by the Original BTSA which took place at the offices of Greenberg Traurig Maher, LLP, 200 Gray’s Inn Road, 7th Floor, London, United Kingdom WC1X 8HF at 10:00 a.m. London time on the Closing Date.

“Combination Product” means a Product that is comprised of or contains a Compound as an active ingredient together with one or more other active ingredients and is sold either as a fixed dose or as separate doses in a single package.

“Compounds” means AZD-2514 and AZD-0914.

“Contract” means any contract, agreement, lease, license or other commitment or arrangement, whether oral or written, that is binding on any Person or any of its property under applicable Law, including all amendments thereto.

“Development” means all activities relating to preparing and conducting preclinical testing, toxicology testing, human clinical studies, regulatory activities (e.g., regulatory applications), formulation, manufacturing process development, scale-up and associated validation, quality assurance and quality control activities and the terms “Develop”, “Developing” and “Developed” shall be construed accordingly.

“Development Costs” means, all costs and expenses actually incurred by a Person (or its Affiliates) or for its account and specifically attributable to its conduct of specific Development activities, which shall include: (a) amounts paid by such Person (or its Affiliates) to Third Parties contracted to conduct clinical trials such as costs for Third Party suppliers of clinical services, clinical site recruiting, training and participation, monitoring of clinical sites, data analysis and data quality assurance, and/or Third-Party costs for preparing, reviewing or developing data and documents for submission to Governmental Authorities; (b) amounts paid for the supply of the Products and comparator drugs for use in clinical trials; and (c) actual direct costs and expenses of such Person’s (or its Affiliates’) internal employees’ actual work in conducting or managing such Development activities (including allocations of direct overheads, but not including allocations of general, corporate or administrative overheads).

“Diligent Efforts” means, with respect to a Company’s obligation under this Agreement relating to any Product, the level of efforts in carrying out such obligation in a sustained manner that is at least consistent with the efforts a similarly situated Person typically devotes to a product of similar commercial and scientific potential at a similar stage in its lifecycle, taking into consideration its safety and efficacy, its cost to develop [*], the competitiveness of alternative Third Party products [*] and the nature and extent of its market exclusivity (including Patent coverage and regulatory exclusivity), the likelihood of regulatory approval, its expected profitability, including the amounts of marketing and promotional expenditures with respect to any Product and all other relevant factors. Diligent Efforts shall be determined individually with respect to appropriate and reasonably defined specific markets or groups of markets, and it is understood that the level of Diligent Efforts required during any specific period may vary from country to country and between different markets or groups of markets. Notwithstanding the foregoing, Diligent Efforts shall not require the performance of any task or activity in any country or region which task or activity would not be commercially reasonable in the opinion of the Board of Directors of the UK Company to perform.

“Employee Benefit Plans” means all pension, retirement, health and welfare benefit plans, including, without limitation, each employee benefit plan, and all other compensation and benefit plans, policies, programs or arrangements, including, without limitation, those providing deferred compensation, incentive compensation, severance or termination pay, retention or change in control compensation, death benefits, or equity-based compensation, in each case, sponsored, maintained or contributed to, or required to be contributed to, by the Sellers for the benefit of employees of the Small Molecule Anti-Infective Program and their beneficiaries and dependents.

“Encumbrance” means any security interest, pledge, hypothecation, mortgage, lien (including environmental and Tax liens), violation, charge, lease, license, encumbrance, servient easement, adverse claim, reversion, reverter, preferential arrangement, restrictive covenant, condition or restriction of any kind, including any restriction on the use, voting, transfer, receipt of income or other exercise of any attributes of ownership, other than any licenses of Patents.

[4] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
any other research or development data), standard operating procedures, manufacturing records, stability data and other study data and procedures.

“Large Molecule Anti-Infective Business” means the business of the Sellers and their respective Affiliates involving anti-infective approaches utilizing biologicals to attack a pathogen or otherwise prevent or treat any infection (including bacterial or viral infections), including biologicals that include (a) antibodies, proteins, vaccines and modified nucleic acids; (b) vaccines for the prevention and/or treatment of respiratory viruses (respiratory syncytial virus and flu); and (c) “novel vaccines” which may include therapeutic vaccines for chronic infections and oncolytic viruses.

“Law” means any federal, national, supranational, state, provincial, local or similar statute, law, ordinance, regulation, rule, treaty, directive, permit, Governmental Order, code, order, rules of stock exchanges, requirement or rule of law (including common law).

“Lease” means the lease agreement for the US Company Premises to be entered into by the US Company and the US Seller at Closing.

“Liabilities” means any and all debts, liabilities and obligations, whether accrued or fixed, absolute or contingent, matured or unmatured or determined or determinable, including those arising under any Law, Action or Governmental Order and those arising under any contract, agreement, arrangement, commitment or undertaking.

“Management Carve-Out Payment Agreement” means the Management Carve-Out Payment Agreement to be entered into by the US Company and the Key Employees at Closing.

“Net Sales” means, with respect to any Product, the gross amount invoiced by the UK Company, its affiliates, or any sublicensee of the UK Company for commercial sales of such Product to third parties (including distributors) less, to the extent included in such invoiced amount: (a) normal and customary trade, quantity or prompt settlement discounts (including chargebacks and allowances actually allowed); (b) amounts repaid or credited by reason of rejection, returns, or recalls of goods, rebates or bona fide price reductions determined by the UK Company or its affiliates in good faith; (c) rebates and similar payments made with respect to sales paid for by any governmental or regulatory authority such as, by way of illustration and not in limitation of the parties’ rights hereunder, Federal or state Medicaid, Medicare or similar state programs in the US or equivalent governmental programs in any other country; (d) any invoiced amounts which are not collected by the UK Company or its affiliates, including bad debts; (e) excise taxes, indirect taxes, customs duties, customs levies and import fees imposed on the sale, importation, use or distribution of Products; (f) any other similar and customary deductions that are consistent with generally accepted accounting principles, or in the case of non-US sales, other applicable accounting standards for the jurisdiction at issue; (g) [*] transportation costs, including insurance and shipping, freight, and handling charges, including distribution expenses, packaging and related insurance charges; and (h) [*], including [*] (it being acknowledged that [*]). Any sales between the UK Company and its affiliates and sublicensees shall be disregarded for purposes of calculating Net Sales, and Net Sales shall be calculated using the UK Company’s
internal audited systems used to report such sales as applied consistently among the UK Company’s products.

“Net Sales Based Term” means, in respect of each Product, on a country-by-country basis, the period commencing on the date of the first commercial sale of the Product in that country and ending on the latest to occur of (a) the expiration of the last to expire of the valid claims of any applicable Company patent rights covering such Product in such country; and (b) the tenth (10th) anniversary of a first commercial sale of a Product in that country.

“Offer Letters” means the employment offer letters and non-disclosure and proprietary rights assignment agreements, in a form acceptable to the Sellers, to be entered into by the US Company and each of the Transferred Employees to be effective as of Closing.

“[*]” means the [*] which can be [*].

“Ordinary Shares” means ordinary shares of $0.20 each in the capital of the UK Company.

“Patents” means all patents (which shall include invention patents, utility models, design patents, industrial designs, and priority rights), applications for patents, invention disclosures, provisional applications, substitutions, supplementary protection certificates, reissues, reexaminations, renewals, revisions, extensions, divisionals, continuations, inventors’ certificates, utility certificates, patents or certificates of addition, inventors’ certificates of addition, and utility certificates of addition and other indices of invention ownership.

“Permitted Encumbrances” means (a) statutory liens for current Taxes not yet due or delinquent (or which may be paid without interest or penalties) or the validity or amount of which is being contested in good faith by appropriate proceedings, (b) mechanics’, carriers’, workers’, repairers’ and other similar liens arising or incurred in the ordinary course of business relating to obligations as to which there is no default on the part of a Seller or a Company, as the case may be, or the validity or amount of which is being contested in good faith by appropriate proceedings, or pledges, deposits or other liens securing the performance of bids, trade contracts, leases or statutory obligations (including workers’ compensation, unemployment insurance or other social security legislation), (c) zoning, entitlement, conservation restriction and other land use and environmental regulations by Governmental Authorities, (d) all covenants, conditions, restrictions, easements, charges, rights-of-way, other Encumbrances and other similar matters of record set forth in any state, local or municipal franchise, and (e) matters which would be disclosed by an accurate survey or inspection of the real property which do not materially impair the occupancy or current use of such real property which they encumber.

“Person” means any individual, partnership, firm, corporation, limited liability company, association, trust, unincorporated organization or other entity, as well as any syndicate or group that would be deemed to be a person under Section 13(d)(3) of the Securities Exchange Act of 1934, as amended.

“Pre-Closing Period” means any taxable period (or portion thereof) ending on or prior to the date of the Closing.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

“Product Liabilities” means, with respect to any Compound or Product, all Liabilities resulting from actual or alleged harm, injury, damage or death to persons, property or business, irrespective of the legal theory asserted.

“Products” means the AZD-2514 Product and the AZD-0914 Product.

“Programs” means those research and Development programs set forth on Section 1.01(b) of the Seller Disclosure Schedule.

“Regulatory Materials” means, with respect to the Compounds, all (a) documentation comprising the INDs and (b) correspondence and reports exclusively related to the Compounds and Programs and necessary, or otherwise limiting the ability to, commercially distribute, sell or market the Compounds and Programs submitted to or received from Governmental Authorities (including minutes and official contact reports relating to any communications with any Governmental Authority) and relevant supporting documents with respect thereto, and (c) all data (including clinical and pre-clinical data) contained in any of the foregoing, in each case ((a), (b) and (c)), to the extent in the possession of or under control of a Seller or any of its Affiliates.

“Research Data” means, to the extent available, (a) the chemical and biological data including chemical structures and all screening assays as found in the Sellers’ databases for such data (IBIS and ISAC, for screening and chemical data respectively), (b) documents stored in the Sellers’ networked shared drives (the L: and M: drives) which include program data and summary reports which are not found in IBIS, including pharmacokinetics (PK) studies and in vivo studies, (c) program files stored on the Sellers’ Sharepoint Datasite, (d) crystallography and molecular modeling data, (e) data that may be found in Sellers’ Corporate Document storage systems (named GEL and ANGEL), and (f) analytical data, including nuclear magnetic resonance (NMR) and mass spectroscopy (MS) data which are used for chemical structural determination, in each case, exclusively relating to the Programs or the Legacy Programs.

“Samples” means a [*] sample of a small molecule compound exclusively relating to a Legacy Program.

“Securities Act” means the Securities Act of 1933, as amended.

“Seller Disclosure Schedule” means the Seller Disclosure Schedule attached hereto, dated as of the date hereof, delivered by the Sellers to the Companies in connection with this Agreement. Notwithstanding anything to the contrary contained in the Seller Disclosure Schedule or in this Agreement, the information and disclosures contained in any section of the Seller Disclosure Schedule shall be deemed to be disclosed and incorporated by reference in any other section of the Seller Disclosure Schedule as though fully set forth in such other section for which the applicability of such information and disclosure is reasonably apparent on the face of such information or disclosure.

“Shareholders’ Agreement” means the shareholders’ agreement entered into by the UK Company and the Sweden Seller at Closing, as amended and restated on or about the date of this Agreement.
“Tax” or “Taxes” means any tax, levy, impost or duty and any similar charge, contribution, withholding or deduction (together with any and all interest, penalties, additions to tax and additional amounts imposed with respect thereto) imposed by any Governmental Authority.

“Tax Returns” means any and all returns, reports and forms (including, elections, declarations, amendments, schedules, information returns or attachments thereto) filed with a Governmental Authority with respect to Taxes.

“Third Party” means any Person other than a Seller, a Company or any of their respective Affiliates.

“Transferred Clinical Materials” shall mean all (a) Compound drug substances, clinical samples and specimens, (b) raw materials, including active pharmaceutical ingredients in bulk form, used to make any Compound, (c) biological materials, reagents, constituents substances, materials, stores and supplies exclusively used with respect to the Compounds or the Programs, in each case, as set forth on Section 1.01(c) of the Seller Disclosure Schedule.

“Transferred Contracts” shall mean the Contracts set forth on Section 1.01(d) of the Seller Disclosure Schedule.

“Transferred Enforcement Rights” means all claims (including claims for past infringement or misappropriation) and causes of action of the Seller against other Persons (regardless of whether or not such claims and causes of action have been asserted by the Seller), and all rights of indemnity, warranty rights, rights of contribution, rights to refunds, rights of reimbursement and other rights of recovery possessed by the Seller (regardless of whether such rights are currently exercisable), in each case, related to the Transferred Intellectual Property.

“Transferred Intellectual Property” shall mean, collectively, (a) the Patents set forth on Section 1.01(e) of the Seller Disclosure Schedule, (b) the Know-How of the Sellers, and (c) the Regulatory Materials, in each case of clauses (b) and (c), solely to the extent the foregoing (i) is protectable under applicable Law and (ii) exclusively relates to the Compounds or the Programs.

“Transferred Tangible Assets” shall mean the tangible personal property assets set forth on Section 1.01(f) of the Seller Disclosure Schedule.

“Transition Services Agreement” means the Transition Services Agreement to be entered into by the UK Company and the applicable Sellers at the Closing.

“US Company Premises” means the office and facility space located in Waltham, Massachusetts in respect of which the US Company will enter into the Lease at Closing.

SECTION 1.02. Definitions. The following terms have the meanings set forth in the Sections set forth below:

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ARTICLE II
TRANSFER OF BUSINESS AND SUBSCRIPTION

SECTION 2.01. Conveyance of Transferred Assets.

(a) Transferred Assets. Upon the terms and subject to the conditions set forth in this Agreement, at the Closing, each Seller shall sell, assign, transfer, convey and deliver, or cause to be sold, assigned, transferred, conveyed and delivered, free and clear of all Encumbrances other than Permitted Encumbrances, all of such Seller’s right, title and interest in and to the following (collectively, the “Transferred Assets”):

(i) to the UK Company, and the UK Company shall purchase from the applicable Sellers, (A) all rights under the Transferred Contracts, (B) the Transferred Intellectual Property, and (C) the Transferred Enforcement Rights; and
(ii) to the US Company, and the US Company shall purchase from the applicable Sellers, (A) the Transferred Clinical Materials and (B) the Transferred Tangible Assets.

(b) Notwithstanding anything in Section 2.01(a) to the contrary, the Sellers shall not sell, convey, assign, transfer or deliver, nor cause to be sold, conveyed, assigned, transferred or delivered, to the Companies, and the Companies shall not purchase, and the Transferred Assets shall not include, any properties, assets and rights of the Sellers and their Affiliates of whatever kind and nature, real, personal or mixed, tangible or intangible (i) to which a Seller’s right, title and interest to are not expressly included in the Transferred Assets, or (ii) if an attempted assignment thereof, without consent of a third party thereto, would constitute a breach or other contravention thereof or in any way adversely affect the rights of a Company or a Seller thereunder (collectively, the “Excluded Assets”). The Excluded Assets shall include, without limitation, the following:

(i) all cash and cash equivalents, securities, and negotiable instruments of a Seller or its Affiliates on hand, in lock boxes, in financial institutions or elsewhere, including all cash residing in any collateral cash account securing any obligation or contingent obligation of a Seller or any of its Affiliates;

(ii) all of the Sellers’ and their respective Affiliates’ accounts receivable, notes and other amounts receivable from Third Parties, including customers, arising solely from the sale of Products before the Closing, whether or not in the ordinary course, together with any unpaid financing charges accrued thereon;

(iii) any rights to Tax refunds, credits, deductions, allowances or other Tax benefits attributable to any Pre-Closing Period;

(iv) the company seal, minute books, charter documents, stock or equity record books and such other books and records as pertain to the organization, existence or capitalization of a Seller and its Affiliates, as well as any other records or materials relating to a Seller or its Affiliates generally and not exclusively related to the Transferred Assets or the operations of the Small Molecule Anti-Infective Program;

(v) all right, title and interest in and to the names “AstraZeneca” and “AZ”;

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[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

(vi) all tangible personal property of a Seller or any of its Affiliates, other than the Transferred Clinical Materials, the Transferred Tangible Assets and the Regulatory Materials included in the Transferred Intellectual Property;

(vii) all real property owned or leased by a Seller or any of its Affiliates, other than, for the avoidance of doubt, the leasehold interest in the US Company Premises that will be acquired by the US Company at Closing pursuant to the Lease;

(viii) all rights of a Seller under this Agreement and the Ancillary Agreements;

(ix) all assets retained by the Sellers and their Affiliates that are necessary for the Sellers to provide the services to the UK Company as contemplated under the Transition Services Agreement;

(x) Tax Returns of a Seller and its Affiliates, other than those relating solely to the Tax treatment of the UK Company or the US Company in respect of the Transferred Assets;

(xi) all Employee Benefit Plans and any assets relating thereto;

(xii) all current and prior insurance policies of a Seller and its Affiliates and all rights of any nature with respect thereto, including all insurance recoveries thereunder and rights to assert claims with respect to any such insurance recoveries; and

(xiii) any right, interest, property or asset that relates to (A) the Excluded Products or (B) the Large Molecule Anti-Infective Business.

SECTION 2.02. Assumption and Exclusion of Liabilities.

(a) Upon the terms and subject to the conditions set forth in this Agreement, the Companies shall, by executing and delivering, at the Closing, the Assignment and Assumption Agreement, jointly and severally, assume, and agree to pay, perform and discharge when due, any and all of the Liabilities of the Sellers exclusively relating to the Small Molecule Anti-Infective Program or the Transferred Assets arising on or after the Closing Date, other than the Excluded Liabilities set forth in Section 2.02(b) below (the “Assumed Liabilities”). The Assumed Liabilities include, but are not limited to, the following:

(i) all Liabilities of a Seller and its Affiliates comprising commitments in respect of Development Costs relating to the Compounds and Programs to the extent such Liabilities relate to the period of time on or after Closing;

(ii) all Liabilities of a Seller and its Affiliates arising under the Transferred Contracts assumed by the Companies;

(iii) all Liabilities arising out of or relating to Actions commenced after the Closing, irrespective of the legal theory asserted, arising from the manufacture, advertising, marketing, distribution, sale or use of the Products or the Compounds, solely

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to the extent relating to the period of time on or after the Closing, including all Liabilities for product warranty service claims relating to the Products and Compounds and all Product Liabilities;

(iv) all Liabilities under the Transferred Contracts to customers, suppliers or other Third Parties for products, materials and services, to the extent relating to the Small Molecule Anti-Infective Program, either (A) ordered in the ordinary course of business prior to the Closing, but scheduled to be delivered or provided after the Closing, which remain unpaid as of the Closing, or (B) the delivery or provision of which was accelerated to occur prior to the Closing in a manner not consistent with past practice and which would otherwise have been an Assumed Liability pursuant to subclause (A) above but for such acceleration;

(v) all other Liabilities arising out of or relating to the return of any Product, including all Liabilities for any chargebacks, credits or rebates in respect of any Product;

(vi) all Taxes relating to the Transferred Assets or the Small Molecule Anti-Infective Program other than Excluded Taxes; and

(vii) all other Liabilities arising out of or relating to the Small Molecule Anti-Infective Program or the Transferred Assets, including the use, ownership, possession, operation, sale or lease of the Transferred Assets, to the extent such Liabilities relate to the period of time on or after Closing.

(b) The Sellers shall retain, and shall be responsible for paying, performing and discharging when due, and the Companies shall not assume or have any responsibility for, the following Liabilities (the “Excluded Liabilities”):

(i) Other than those Liabilities described in Section 2.02(a)(iv), all Liabilities of a Seller and its Affiliates in respect of any and all accounts payables to the extent such Liabilities relate to the period of time prior to the Closing;

(ii) all Excluded Taxes;

(iii) all Liabilities relating to or arising out of the Employee Benefit Plans or the Transferred Employees relating to the period of time prior to the Closing;

(iv) all Liabilities relating to or arising out of the Excluded Assets;

(v) all Liabilities relating to the Transferred Contracts to the extent such obligations (A) arise before the Closing Date, (B) arise from or relate to any breach by the Sellers of any provision of any of such contracts, or (C) arise from or relate to any event, circumstance or condition occurring or existing on or prior to the Closing Date that, with notice or lapse of time, would constitute or result in a breach of any of such contracts;

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As consideration for the Transferred Clinical Materials, at Closing, the US Company shall pay to the US Seller $[*] (the “Clinical Materials Purchase Price”).

As consideration for the Transferred Intellectual Property, at Closing, the UK Company shall pay an aggregate amount equal to $[*] (the “Intellectual Property Purchase Price”), [*] of which shall be paid to the UK Seller and [*] of which shall be paid to the Sweden Seller.

In addition, the Sweden Seller shall receive a one-time non-refundable payment of $10,000,000 (the “Milestone Payment”) upon first achievement of a First Commercial Sale (the “Milestone”). The Milestone payment shall be made within 24 months of the First Commercial Sale, and at the UK Company’s sole election, the Milestone may be paid (i) in cash by wire transfer of immediately available funds or (ii) by the issuance to the Sweden Seller of such number of Ordinary Shares as shall be equal to $10,000,000 divided by the then current fair market value of one Ordinary Share, as determined in good faith by the UK Company’s Board of Directors. Notwithstanding the foregoing, if the payment of the Milestone at the time set forth above is deemed by the UK Company’s Board of Directors to be significantly burdensome to the UK Company, then the UK Company and the Sweden Seller shall explore in good faith modifying the time for the payment of the Milestone. Following the Sweden Seller’s receipt of the Milestone Payment, the Sweden Seller shall pay to the UK Seller [*] of the Milestone Payment. Following the occurrence of the Milestone, no dividend, return of capital or other distribution shall be made by the UK Company to any shareholder until the Milestone Payment has been made in full.

In addition, the UK Company shall pay to the UK Seller and the Sweden Seller royalties (the “Royalties”) on Net Sales of the Products, as set forth on Exhibit 2.05(e), [*] of which shall be paid to the UK Seller and [*] of which shall be paid to the Sweden Seller.

SECTION 2.06. Closing. Closing took place on May 11, 2015 (the “Closing Date”) pursuant to the Original BTSA.

SECTION 2.07. Closing Deliveries by the Sellers. At the Closing, the Sellers shall deliver or cause to be delivered:

(a) to the UK Company, an amount in U.S. dollars equal to the Subscription Price by wire transfer in immediately available funds to an account designated by the UK Company at least [*] Business Day prior to Closing;

(b) to the Companies, the Assignment of Transferred Intellectual Property, the Bill of Sale and such other instruments to effect the transfer of the Transferred Assets to the Companies or evidence such transfer, in each case duly executed by the appropriate Seller; and

(c) to the Companies, executed counterparts of each other Ancillary Agreement to which a Seller is a party.

SECTION 2.08. Closing Deliveries by the Companies. At the Closing:

(a) the UK Company shall enter the Sweden Seller in the register of members of the UK Company as the holder of the UK Company Shares and issue a certificate or certificates to the Sweden Seller representing its holding of the UK Company Shares;

(b) the UK Company shall deliver to the US Company an amount in U.S. dollars equal to the aggregate sum of (i) the Tangible Asset Purchase Price plus (ii) the Clinical Materials Purchase Price, by wire transfer in immediately available funds to an account designated by the US Company at least [*] Business Day prior to Closing;

(c) the US Company shall deliver to the US Seller, an amount in U.S. dollars equal to the aggregate sum of (i) the Tangible Asset Purchase Price plus (ii) the Clinical Materials Purchase Price, by wire transfer in immediately available funds to an account designated by the US Seller at least [*] Business Day prior to Closing;

(d) the UK Company shall deliver to (i) the UK Seller, an amount in U.S. dollars equal to [*] of the Intellectual Property Purchase Price and (ii) the Sweden Seller, an amount in U.S. dollars equal to [*] of the Intellectual Property Purchase Price, in each case, by wire transfer in immediately available funds to an account designated by the UK Seller and the Sweden Seller, respectively, at least [*] Business Day prior to Closing;

(e) the US Company shall deliver to the Sweden Seller fully executed copies of the Employment Agreements and the Offer Letters; and

(f) each Company shall deliver to the Sweden Seller executed counterparts of each Ancillary Agreement to which such Company is a party.

ARTICLE III

REPRESENTATIONS AND WARRANTIES
OF THE SELLERS

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
Agreement has been, and upon their execution the Ancillary Agreements to which a Company is a party shall have been, duly executed and delivered by each Company, the performance by each Company of its obligations hereunder and thereunder and the consummation by each Company of the transactions contemplated hereby and thereby. The execution and delivery of this Agreement and the Ancillary Agreements by each Seller, the performance by each Seller of its obligations hereunder and thereunder and the consummation by each Seller of the transactions contemplated hereby and thereby have been duly authorized by all requisite action on the part of each Company and its equity holders.

Each Company is duly licensed or qualified to do business and is in good standing (to the extent such concept is recognized by the applicable jurisdiction) under the laws of the jurisdiction of its organization and has all necessary power and authority to enter into this Agreement and the Ancillary Agreements, to carry out its obligations hereunder and thereunder and to consummate the transactions contemplated hereby and thereby. Each Seller is duly organized, validly existing and in good standing (to the extent such concept is recognized by the applicable jurisdiction) under the laws of the jurisdiction of its organization and has all necessary power and authority to enter into this Agreement and the Ancillary Agreements, to carry out its obligations hereunder and thereunder and to consummate the transactions contemplated hereby and thereby. Each Seller is duly organized, validly existing and in good standing (to the extent such concept is recognized by the applicable jurisdiction) in each jurisdiction in which the properties owned or leased by it or the operation of its business makes such licensing or qualification necessary, except to the extent that the failure to so licensed, qualified or in good standing would not materially and adversely affect the ability of such Seller to carry out its obligations under this Agreement and the Ancillary Agreements or prevent such Seller from consummating the transactions contemplated hereby and thereby. The execution and delivery of this Agreement and the Ancillary Agreements by each Seller, the performance by each Seller of its obligations hereunder and thereunder and the consummation by each Seller of the transactions contemplated hereby and thereby have been duly authorized by all requisite action on the part of each Seller and its equity holders. This Agreement has been, and upon their execution, the Ancillary Agreements shall have been, duly executed and delivered by each Seller, and (assuming due authorization, execution and delivery by the Companies) this Agreement constitutes, and upon their execution the Ancillary Agreements shall constitute, legal, valid and binding obligations of each Seller, enforceable against each Seller in accordance with their respective terms.
SECTION 4.02. No Conflict. The execution, delivery and performance by each Company of this Agreement and the Ancillary Agreements to which it is a party do not and will not (a) violate, conflict with or result in the breach of any provision of the certificate of incorporation, bylaws or articles of association (or similar organizational or constitutional documents) of such Company, (b) conflict with or violate any Law or Governmental Order applicable to such Company or its respective assets, properties or businesses or (c) conflict with, result in any breach of, constitute a default (or event which with the giving of notice or lapse of time, or both, would become a default) under, require any consent under, or give rise to a right of termination, amendment, acceleration, suspension, revocation or cancellation of, any note, bond, mortgage or indenture, contract, agreement, lease, sublease, license, permit, franchise or other instrument or arrangement to which such Company is a party, except, in the case of clauses (b) and (c), as would not materially and adversely affect the ability of such Company to carry out its obligations under this Agreement and the Ancillary Agreements or prevent such Company from consummating the transactions contemplated hereby and thereby.

SECTION 4.03. Capitalization.

(a) The issued share capital of the UK Company consists of 100 Ordinary Shares. Immediately preceding the date hereof, no other shares were outstanding. Upon consummation of the transactions contemplated by this Agreement, the Sweden Seller will own 100% of the outstanding A Preference Shares and 100% of the Ordinary Shares. There is no Encumbrance in relation to any of the A Preference Shares or unissued shares in the capital of the UK Company and, other than this Agreement, there is no agreement or arrangement which give rise to or create any such Encumbrance or right to receive A Preference Shares or any other shares in the capital of the UK Company. No Person has claimed to be entitled to an Encumbrance in relation to any A Preference Shares or any unissued shares in the capital of the UK Company.

(b) The authorized capital stock of the US Company consists of 100 shares of common stock, par value $0.01 per share, all of which, as of the date hereof, are issued and outstanding, are validly issued, fully paid and nonassessable, and are owned of record and beneficially by the UK Company free and clear of all Encumbrances (other than Permitted Encumbrances).

SECTION 4.04. Authorization. The UK Company Shares have been duly and validly authorized for issuance and sale to the Sweden Seller pursuant to this Agreement and, when the UK Company Shares are issued and delivered by the UK Company as consideration therefor in accordance with the terms of this Agreement, the UK Company Shares will be duly and validly issued and fully paid and nonassessable, and will be sold free and clear of any Encumbrance. No further approval or authorization of any stockholder, the board of directors of the UK Company or others is required for the issuance and sale or transfer of the UK Company Shares.

SECTION 4.05. No Prior Operations. The UK Company was incorporated under the laws of England and Wales on March 6, 2015. The US Company was incorporated under the laws of Delaware on March 11, 2015. Neither Company had any operations prior to Closing, has generated any revenues and has any Liabilities.

ARTICLE V

ADDITIONAL AGREEMENTS

SECTION 5.01. Setup Costs. Notwithstanding anything in this Agreement to the contrary, [*] costs and expenses incurred in connection with (a) any activities that are related to the establishment of the Companies or are otherwise necessary for the Companies in connection with the transactions contemplated by this Agreement and (b) transferring the Transferred Assets and the Assumed Liabilities to the Companies including the costs and expenses relating to the physical transportation and delivery of the Transferred Clinical Materials to the Companies.

SECTION 5.02. Transition Services and Other Ancillary Agreements. Following the Closing, the Sweden Seller shall provide, or cause to be provided, to the UK Company those transition services specifically set forth in the Transition Services Agreement. At the Closing, the Sellers and the Companies shall, or shall cause their respective Affiliates to, enter into the Ancillary Agreements to which they are parties.

SECTION 5.03. Tax Matters.

(a) Unless specifically provided otherwise in this Agreement, any party receiving payments under this Agreement shall pay any and all Taxes levied on account of all

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otherwise to any relief or exemption from any applicable withholding Tax, the other parties shall provide such assistance or cooperation as such party may reasonably request for the purpose of claiming or obtaining the benefit of such relief or exemption.

(b) All amounts payable under this Agreement are stated exclusive of Indirect Taxes. If any Indirect Taxes are chargeable in respect of any such payments, the paying party shall pay such Indirect Taxes (or an amount equal thereto, as the case may be) at the applicable rate in respect of any such payments, on the due date of such payments to which such Indirect Taxes relate. Each party hereto shall issue its invoices for all amounts payable under this Agreement consistent with Indirect Tax requirements and irrespective of whether the sums may be netted for settlement purposes. Each such invoice shall state separately the amount of Indirect Taxes chargeable in respect of the payments to which invoice relates.

(c) Unless specifically provided otherwise in this Agreement, the Companies shall be responsible for all Taxes, if any, imposed in connection with this Agreement or the Transferred Assets, other than any Taxes imposed on the Sellers in respect of any income received and retained by the Sellers under this Agreement. If the Sellers or any of their respective Affiliates are required to pay such Taxes, the Companies shall promptly reimburse the Sellers therefor on an after-Tax basis.

SECTION 5.04. Business Confidential Information.

(a) Following the Closing, the Companies shall, and shall cause their respective Affiliates to, treat and hold any proprietary and confidential information of the Sellers and their respective Affiliates that is not included within the Transferred Assets (collectively, the "Business Confidential Information") with at least the same degree of care, but no less than reasonable care, with which it protects its own confidential information.

(b) The obligations of confidentiality contained in Section 5.04(a) with respect to the Business Confidential Information shall not apply to any information to the extent that (i) it is already, or becomes, publicly available or otherwise part of the public domain after the Closing Date, and other than through any fault of a Company or any of its Affiliates in breach of this Agreement, (ii) it is disclosed to a Company or any of its Affiliates after the Closing Date, other than under an obligation of confidentiality, by a Third Party who has no obligation of any nature to the Sellers not to disclose such information to others or (iii) it is acquired or developed independently by a Company after the Closing Date without reference to any Business Confidential Information in possession of such Company or any of its Affiliates as of immediately prior to the Closing.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

SECTION 5.05. Publicity. The Companies shall not issue any press releases or make other public statements or disclosures regarding the subject matter of this Agreement, the Ancillary Agreements and the transactions contemplated hereby and thereby without the prior written consent of the Sellers.

SECTION 5.06. Wrong Pockets. For a period of up to [*] from and after the Closing Date, if either any Company or any Seller becomes aware that any of the Transferred Assets has not been transferred to the Companies or that any of the Excluded Assets has been transferred to a Company, it shall promptly notify the other and the Companies and the Sellers shall, as soon as reasonably practicable, ensure that such property is transferred, with any necessary prior Third-Party consent or approval, to (a) a Company, at the expense of the Sellers, in the case of any Transferred Asset which was not transferred to such Company at the Closing; or (b) the Sellers, at the expense of the Companies, in the case of any Excluded Asset which was transferred to a Company at the Closing.

SECTION 5.07. Indemnification.

(a) The Companies and their respective Affiliates (other than the Sellers), and their officers, directors, employees, agents, successors and assigns shall be indemnified and held harmless by each Seller, severally and not jointly, for and against all losses, damages, claims, costs and expenses, interest, awards, judgments and penalties (including reasonable attorneys’ and consultants’ fees and expenses) actually suffered or incurred by them arising after Closing out of or resulting from any Excluded Asset or Excluded Liability.

(b) The Sellers and their respective Affiliates (other than the Companies), their officers, directors, employees, agents, successors and assigns shall be indemnified and held harmless by each Company, severally and not jointly, for and against any and all losses, damages, claims, costs and expenses, interest, awards, judgments and penalties (including

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
SECTION 5.08. Further Assurances. From time to time after the date of this Agreement, upon request of any party, each party shall execute, acknowledge and deliver all such other instruments and documents and shall take all such other actions required to consummate and make effective the transactions contemplated by this Agreement and the Ancillary Agreements.

SECTION 5.09. Legacy Programs.

(a) From time to time after the Closing Date until [*], plus an additional period of [*], upon the prior written request of the UK Company, the Sellers shall provide the Companies, at no additional cost or expense, with Samples, Biological Tools and Research Data, to the extent in the possession of the Sellers, relating to any of the Sellers’ legacy research and development programs set forth on Section 5.09(a) of the Seller Disclosure Schedule (the “Legacy Programs”); provided, that, (i) [*]; (ii) prior to the Sellers delivering any such Samples, Biological Tools or Research Data, the UK Company and the Sellers shall enter into a mutually agreed upon confidentiality agreement pursuant to which the Companies will agree to keep all such Samples, Biological Tools and Research Data confidential and (iii) the Companies shall use such Samples, Biological Tools and Research Data solely for the purpose of conducting the Small Molecule Anti-Infective Program.

(b) Notwithstanding anything to the contrary set forth in Section 5.09(a), if, within [*] after the end of the time period described in the first sentence of Section 5.09(a), [*] relating to any Legacy Program, (i) upon [*], [*] the Samples, Biological Tools and Research Data relating to such Legacy Program that [*] pursuant to Section 5.09(a) and (ii) [*] any Samples, Biological Tools and Research Data relating to such Legacy Program shall [*]; provided, that, [*] the Samples, Biological Tools and Research Data relating to such Legacy Program if such Legacy Program is [*] or [*]. In no event [*] any Samples, Biological Tools and Research Data pursuant to this Section 5.09(b) [*] pursuant to Section 5.09(a).

(c) If, prior to receiving a request from the Companies pursuant to Section 5.09(a), and only during the time period described in the first sentence of Section 5.09(a), the Seller [*] Samples, Biological Tools and Research Data relating one or more Legacy Program(s) for the purposes of [*], the Seller shall first offer the same to the Companies and provide them a [*] period in which to [*] elect to request access to the Legacy Program(s) pursuant to Section 5.09(a). The Companies acknowledge that failure to respond to the Seller’s offer in a timely manner results in the termination of the same, and the Seller will be free to [*]. Failure to make a request for Legacy Program access in response to an opportunity as described in Section 5.09(c) herein will not preclude the Companies from filing a request under Section 5.09(a) at a later point in time.

SECTION 5.10. Document Retention. If, following Closing, the Sellers determine, in accordance with the Sellers’ internal document retention policy then in effect, to destroy any of the Sellers’ documents, data or other information on any tangible medium

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
(c) The UK Company shall maintain complete and accurate records of all of its and its Affiliates’ and sublicensees’ sales of Products in sufficient detail to permit the Sellers to confirm, using standard audit practices, the accuracy of the calculation of Net Sales of Products set forth in each Net Sales Statement. Upon reasonable prior notice, such records shall be available to the Sellers during regular business hours for a period of [*] from the end of the calendar year in which such individual records were created, for examination, at the expense of the Sellers, and not more often than [*], by an independent certified public accountant selected by the Sellers and reasonably acceptable to the UK Company, for the sole purpose of verifying the accuracy of Net Sales Statements. Any such auditor shall not disclose any Business Confidential Information, except to the extent such disclosure is necessary to verify the accuracy of the Net Sales Statements furnished by the UK Company. Any amounts shown to have been overpaid shall be refunded within [*] from the accountant’s report. The Sellers shall bear the full cost of such audit unless such audit discloses an underpayment of the amount actually owed during the applicable Calendar Quarter of more than [*], in which case the UK Company shall bear the reasonable cost of such audit.

ARTICLE VI
EMPLOYEE MATTERS

SECTION 6.01. Offer of Employment. As of the Closing, the US Company shall have offered employment to each of the employees of the Sellers set forth on Section 6.01 of the Seller Disclosure Schedule (the “Designated Employees”). As used herein, “Transferred Employee” means each Designated Employee who accepts such offer.

SECTION 6.02. Employee Benefits. Effective as of the Closing Date, each Transferred Employee shall cease to be covered under the Employee Benefit Plans. The US Company shall (a) recognize the service completed by the Transferred Employees with the Sellers and their respective Affiliates for purposes of determining eligibility, vesting and benefit accrual service under any employee benefit plan, program or arrangement maintained by the US Company for their employees on or after the Closing Date, and (b) assume responsibility to provide the vacation time, personal days and sick leave benefits due to the Transferred Employees as of the Closing Date; provided, however, that to the extent any cash payments are due to any such Transferred Employees in connection with such benefits described in this clause (b) as of the Closing Date, the Sellers shall be responsible for all such payments.

ARTICLE VII
GENERAL PROVISIONS

SECTION 7.01. Survival. No representations and warranties of the Sellers or the Companies set forth in Articles III and IV of this Agreement shall survive the Closing, or, to the extent given on the date of this Agreement, the date hereof. All other covenants and agreements of the Sellers and the Companies contained herein shall survive the Closing in accordance with their terms.

SECTION 7.02. Expenses. Except as otherwise specified in this Agreement, all costs and expenses, including fees and disbursements of counsel, financial advisors and accountants, incurred in connection with this Agreement and the transactions contemplated by this Agreement shall be paid by the party incurring such costs and expenses, whether or not the Closing shall have occurred.

SECTION 7.03. Notices. All notices, requests, consents, claims, demands, waivers and other communications hereunder shall be in writing and shall be deemed to have been given (a) when delivered by hand (with written confirmation of receipt); (b) when received by the addressee if sent by a nationally recognized overnight courier (receipt requested); (c) on the date sent by facsimile or e-mail of a PDF document (with confirmation of transmission) if sent during normal business hours of the recipient, and on the next Business Day if sent after normal business hours of the recipient; or (d) on the third day after the date mailed, by certified or registered mail, return receipt requested, postage prepaid. Such communications must be sent to the respective parties at the following addresses (or at such other address for a party as shall be specified in a notice given in accordance with this Section 7.02):

(a) if to a Seller:

c/o AstraZeneca UK Limited
Mereside
Alderley Park
Macclesfield, Cheshire SK10 4TG
England

E-mail: [*]  
Attention: Deputy General Counsel, Corporate

with a copy to:

Greenberg Traurig Maher LLP
200 Gray’s Inn Road, 7th Floor
SECTION 7.04. **Severability.** If any term or other provision of this Agreement is invalid, illegal or incapable of being enforced by any Law or public policy, all other terms and provisions of this Agreement shall nevertheless remain in full force and effect for so long as the economic or legal substance of the transactions contemplated by this Agreement is not affected in any manner materially adverse to either party hereto. Upon such determination that any term or other provision is invalid, illegal or incapable of being enforced, the parties hereto shall negotiate in good faith to modify this Agreement so as to effect the original intent of the parties as closely as possible in an acceptable manner in order that the transactions contemplated by this Agreement are consummated as originally contemplated to the greatest extent possible.

SECTION 7.05. **Entire Agreement.** This Agreement and the Ancillary Agreements constitute the entire agreement of the parties hereto with respect to the subject matter hereof and thereof and supersede all prior agreements and undertakings, both written and oral, between the Sellers and the Companies with respect to the subject matter hereof and thereof.

SECTION 7.06. **Assignment.** This Agreement may not be assigned by operation of law or otherwise without the express written consent of the Sellers and the Companies (which consent may be granted or withheld in the sole discretion of the Sellers or the Companies), as the case may be; provided, however, that a Seller may assign this Agreement or any of its rights and obligations hereunder to one or more Affiliates of such Seller without the consent of the Companies.

SECTION 7.07. **Amendment.** This Agreement may not be amended or modified except (a) by an instrument in writing signed by, or on behalf of, a Seller and the UK Company, provided that the UK Company has been duly authorized to enter into such amendments in accordance with the Shareholders’ Agreement or (b) by a waiver in accordance with Section 7.08.

SECTION 7.08. **Waiver.** Either party to this Agreement may (a) extend the time for the performance of any of the obligations or other acts of the other party, (b) waive any inaccuracies in the representations and warranties of the other party contained herein or in any document delivered by the other party pursuant hereto; or (c) waive compliance with any of the agreements of the other party or conditions to such party’s obligations contained herein. Any such extension or waiver shall be valid only if set forth in an instrument in writing signed by the party to be bound thereby, and provided that, in case of the UK Company, the UK Company has been duly authorized to enter into such extension or waiver in accordance with the Shareholders’ Agreement. Any waiver of any term or condition shall not be construed as a waiver of any subsequent breach or a subsequent waiver of the same term or condition, or a waiver...
of any other term or condition of this Agreement. The failure of either party hereto to assert any of its rights hereunder shall not constitute a waiver of any of such rights.

SECTION 7.09. **No Third Party Beneficiaries.** This Agreement shall be binding upon and inure solely to the benefit of the parties hereto and their respective successors and permitted assigns and nothing herein, express or implied, is intended to or shall confer upon any other Person any legal or equitable right, benefit or remedy of any nature whatsoever, including any rights of employment for any specified period, under or by reason of this Agreement.

SECTION 7.10. **Currency.** Unless otherwise specified in this Agreement, all references to currency, monetary values and dollars set forth herein shall mean United States (U.S.) dollars and all payments hereunder shall be made in United States dollars.

SECTION 7.11. **GOVERNING LAW; JURISDICTION.** This AGREEMENT AND ALL CLAIMS OR CAUSES OF ACTION (WHETHER AT LAW, IN CONTRACT, IN TORT OR OTHERWISE) THAT MAY BE BASED UPON, ARISE OUT OF OR RELATE TO THIS AGREEMENT OR THE NEGOTIATION, EXECUTION OR PERFORMANCE HEREOF SHALL BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH THE INTERNAL LAWS OF [*], APPLICABLE TO AGREEMENTS MADE AND TO BE PERFORMED ENTIRELY WITHIN [*], WITHOUT REGARD TO THE CONFLICTS OF LAW PRINCIPLES OF [*]. All Actions arising out of or relating to this Agreement shall be heard and determined exclusively in [*]; provided, however, that if [*] does not have jurisdiction over such Action, such Action shall be heard and determined exclusively in [*]. Consistent with the preceding sentence, the parties hereto hereby (a) submit to the exclusive jurisdiction of [*] for the purpose of any Action arising out of or relating to this Agreement brought by either party hereto and (b) irrevocably waive, and agree not to assert by way of motion, defense, or otherwise, in any such Action, any claim that it is not subject personally to the jurisdiction of the above-named courts, that its property is exempt or immune from attachment or execution, that the Action is brought in an inconvenient forum, that the venue of the Action is improper, or that this Agreement or the transactions contemplated by this Agreement may not be enforced in or by any of the above-named courts.

SECTION 7.12. **WAIVER OF JURY TRIAL.** EACH OF THE PARTIES HERETO HEREBY WAIVES TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW ANY RIGHT IT MAY HAVE TO A TRIAL BY JURY WITH RESPECT TO ANY LITIGATION DIRECTLY OR INDIRECTLY ARISING OUT OF, UNDER OR IN CONNECTION WITH THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED BY THIS AGREEMENT. EACH OF THE PARTIES HERETO HEREBY (A) CERTIFIES THAT NO REPRESENTATIVE, AGENT OR ATTORNEY OF THE OTHER PARTY HAS REPRESENTED, EXPRESSLY OR OTHERWISE, THAT SUCH OTHER PARTY WOULD NOT, IN THE EVENT OF LITIGATION, SEEK TO ENFORCE THE FOREGOING WAIVER AND (B) ACKNOWLEDGES THAT IT HAS BEEN INDUCED TO ENTER INTO THIS AGREEMENT AND THE TRANSACTIONS CONTEMPLATED BY THIS AGREEMENT, AS APPLICABLE, BY, AMONG OTHER THINGS, THE MUTUAL WAIVERS AND CERTIFICATIONS IN THIS SECTION 7.12.

SECTION 7.13. **Specific Performance.** The parties agree that irreparable damage would occur if any provision of this Agreement were not performed in accordance with the terms hereof and that the parties shall be entitled to specific performance of the terms hereof, in addition to any other remedy to which they are entitled at law or in equity.

SECTION 7.14. **Counterparts.** This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together shall be deemed to be one and the same agreement. A signed copy of this Agreement delivered by facsimile, e-mail or other means of electronic transmission shall be deemed to have the same legal effect as delivery of an original signed copy of this Agreement.

(Remainder of page intentionally left blank)

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
EXHIBIT 1.01(A)

FORM OF ASSIGNMENT OF TRANSFERRED INTELLECTUAL PROPERTY

This ASSIGNMENT OF TRANSFERRED INTELLECTUAL PROPERTY (this “Assignment”) is entered into as of , (the “Effective Date”), by and between ASTRAZENECA AB (PUBL), a company incorporated in Sweden under no. 556011-7482 (the “Assignor”), and ENTASIS THERAPEUTICS LIMITED, a private limited company incorporated in England and Wales (the “Assignee”).

WHEREAS, the Assignor wishes to sell, convey, transfer, assign and deliver to the Assignee all of the intellectual property as set forth in Schedule A to this Assignment (the “Transferred Intellectual Property”), including, without limitation, all goodwill symbolized thereby and associated therewith, and the Assignee wishes to purchase, acquire and accept from the Assignor such Transferred Intellectual Property.

NOW, THEREFORE, in consideration of the promises and the consideration hereinafter set forth, the Assignee and the Assignor hereby agree as follows:

1. Assignment of Transferred Intellectual Property; Power of Attorney.

(a) The Assignor hereby perpetually and irrevocably assigns to the Assignee (i) all of the Assignor’s right, title and interest in, to and under the Transferred Intellectual Property and all goodwill symbolized thereby and associated therewith and including all rights therein provided by international conventions and treaties, and the right to sue for past, present and future infringement thereof, (ii) any and all rights of the Assignor to sue at law or in equity for any infringement, imitation, impairment, distortion, dilution or other unauthorized use or conduct in derogation of such Transferred Intellectual Property, including the right to receive all proceeds and damages therefrom, (iii) any and all rights to royalties, profits, compensation, license fees or other payments or remuneration of any kind relating to such Transferred Intellectual Property, and (iv) any and all rights to obtain renewals, reissues, and extensions of registrations or other legal protections pertaining to such Transferred Intellectual Property.

(b) The Assignor shall take all actions necessary to effectuate the assignment of the Transferred Intellectual Property contemplated hereunder, including but not limited to, making filings and executing any documents that may be necessary or desirable for purposes of recordation by the United States Patent and Trademark Office or any other office or authority responsible for registration of Intellectual Property in any other jurisdiction throughout the world. In the event that the Assignor does not take in a timely fashion any action reasonably deemed necessary or advisable by the Assignee, the Assignee shall have the right to take such action. The Assignor hereby grants to the Assignee an irrevocable power of attorney, coupled with an interest, to take all action contemplated or authorized pursuant to this Section 1 including, but not limited to, filings which may be necessary or desirable for purposes of recordation by the United States Patent and Trademark Office or any other office or authority responsible for registration of Intellectual Property in any other jurisdiction throughout the world.

[⁎] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

2. Further Assurances. Each party hereto shall execute and deliver all such other instruments and documents and shall take all such other actions required to consummate and make effective the transactions contemplated by contemplated by this Assignment, including, but not limited to, the execution and delivery of any additional, separate documents and performance of other additional acts necessary or desirable to record and perfect the interest of the Assignee in and to the Transferred Intellectual Property.

[⁎] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
3. **Amendment.** This Assignment may not be amended or modified except by an instrument in writing signed by, or on behalf of, the Assignor and the Assignee.

4. **No Third Party Beneficiaries.** This Assignment shall be binding upon and inure solely to the benefit of the parties hereto and their respective successors and permitted assigns and nothing herein, express or implied, is intended to or shall confer upon any other Person any legal or equitable right, benefit or remedy of any nature whatsoever, including any rights of employment for any specified period, under or by reason of this Assignment.

5. **Severability.** If any term or other provision of this Assignment is invalid, illegal or incapable of being enforced by any law or public policy, all other terms and provisions of this Assignment shall nevertheless remain in full force and effect for so long as the economic or legal substance of the transactions contemplated by this Assignment is not affected in any manner materially adverse to either party hereto. Upon such determination that any term or other provision is invalid, illegal or incapable of being enforced, the parties hereto shall negotiate in good faith to modify this Assignment so as to effect the original intent of the parties as closely as possible in an acceptable manner in order that the transactions contemplated by this Assignment are consummated as originally contemplated to the greatest extent possible.

6. **Governing Law.** This Assignment and all claims or causes of action (whether at law, in contract, in tort or otherwise) that may be based upon, arise out of or relate to this Assignment or the negotiation, execution or performance hereof shall be governed by and construed in accordance with the internal laws of the [*] applicable to agreements made and to be performed entirely within such state, without regard to the conflicts of law principles of such state.

7. **Counterparts.** This Assignment may be executed in counterparts, each of which shall be deemed an original, but all of which together shall be deemed to be one and the same agreement. A signed copy of this Assignment delivered by facsimile, e-mail or other means of electronic transmission shall be deemed to have the same legal effect as delivery of an original signed copy of this Assignment.

   [Signature page follows.]

[= Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.]

---

**IN WITNESS WHEREOF,** the parties have executed, or caused to be executed by their respective officers duly authorized, this Assignment as of the date first written above.

ASTRAZENECA AB (PUBL)

By: 
Name: 
Title: 

ENTASIS THERAPEUTICS LIMITED

By: 
Name: 
Title: 

[= Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.]

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**SCHEDULE A**

**Transferred Intellectual Property**

[= Five pages of certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.]

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**EXHIBIT 1.01(B)**
FORM OF ASSIGNMENT AND ASSUMPTION AGREEMENT
This ASSIGNMENT AND ASSUMPTION AGREEMENT (this “Agreement”) is entered into as of , (the “Effective Date”), by and among AstraZeneca AB (Publ), a company incorporated in Sweden under no. 556011-7482, AstraZeneca UK Limited, a company incorporated in England under no. 3674842, AstraZeneca Pharmaceuticals LP, a Delaware limited partnership (collectively, the “Sellers”), and Entasis Therapeutics Limited, a private limited company incorporated in England and Wales (the “Purchaser”).

WHEREAS, the Sellers and the Purchaser are party to that certain Business Transfer and Subscription Agreement, dated the date hereof, (the “Business Transfer and Subscription Agreement”; unless otherwise defined herein, capitalized terms shall be used herein as defined in the Business Transfer and Subscription Agreement); and WHEREAS, the execution and delivery of this Agreement by the Sellers is required in connection with the consummation of the transactions contemplated by the Business Transfer and Subscription Agreement.

NOW, THEREFORE, in consideration of the promises and the consideration hereinafter set forth, the Purchaser and the Sellers hereby agree as follows:

1. Assignment of the Transferred Contracts. The Sellers hereby sell, assign, transfer, convey and deliver to the Purchaser and its successors and assigns, forever, the entire right, title and interest of the Sellers in and to all of the Transferred Contracts.

2. Assumption of Liabilities. The Purchaser hereby assumes, and agrees to pay, perform and discharge when due, all of the Liabilities of the Sellers and its Affiliates arising under, the Transferred Contracts.

3. Further Assurances. The Sellers hereby covenant and agree that, at any time and from time to time after the date of this Agreement, at the Purchaser’s request, the Sellers will do, execute, acknowledge and deliver, or will cause to be done, executed, acknowledged and delivered, any and all further acts, conveyances, transfers, assignments, and assurances as necessary to implement the intentions of this Agreement.

4. Amendment. This Agreement may not be amended or modified except by an instrument in writing signed by, or on behalf of, the Sellers and the Purchaser.

5. No Third Party Beneficiaries. This Agreement shall be binding upon and inure solely to the benefit of the parties hereto and their respective successors and permitted assigns and nothing herein, express or implied, is intended to or shall confer upon any other Person any legal or equitable right, benefit or remedy of any nature whatsoever, including any rights of employment for any specified period, under or by reason of this Agreement.

6. Severability. If any term or other provision of this Agreement is invalid, illegal or incapable of being enforced by any Law or public policy, all other terms and provisions of this Agreement shall nevertheless remain in full force and effect for so long as the economic or legal substance of the transactions contemplated by this Agreement is not affected in any manner materially adverse to either party hereto. Upon such determination that any term or other provision is invalid, illegal or incapable of being enforced, the parties hereto shall negotiate in good faith to modify this Agreement so as to effect the original intent of the parties as closely as possible in an acceptable manner in order that the transactions contemplated by this Agreement are consummated as originally contemplated to the greatest extent possible.

7. Governing Law. This Agreement and all claims or causes of action (whether at Law, in contract, in tort or otherwise) that may be based upon, arise out of or relate to this Agreement or the negotiation, execution or performance hereof shall be governed by and construed in accordance with the internal Laws of the [*] applicable to agreements made and to be performed entirely within such state, without regard to the conflicts of Law principles of such state.

8. Counterparts. This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together shall be deemed to be one and the same agreement. A signed copy of this Agreement delivered by facsimile, e-mail or other means of electronic transmission shall be deemed to have the same legal effect as delivery of an original signed copy of this Agreement.

[Signature page follows.]

IN WITNESS WHEREOF, the parties have executed, or caused to be executed by their respective officers duly authorized, this Agreement as of the date first written above.

AstraZeneca AB (Publ)

By:

Name:

Title:

AstraZeneca UK Limited
EXHIBIT 1.01(C)

DESCRIPTION OF AZD-0914

[*]

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

EXHIBIT 1.01(D)

DESCRIPTION OF AZD-2514

[*]

[*] = One page of certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

EXHIBIT 1.01(E)

FORM OF BILL OF SALE

This BILL OF SALE (this “Bill of Sale”), is entered into as of , (the “Effective Date”), by and among ASTRAZENECA AB (PUBL), a company incorporated in Sweden under no. 556011-7482, ASTRAZENECA UK LIMITED, a company incorporated in England under no. 3674842, ASTRAZENECA PHARMACEUTICALS LP, a Delaware limited partnership (collectively, the “Sellers”), and ENTASIS THERAPEUTICS INC., a Delaware corporation (the “Purchaser”).

WHEREAS, the Sellers and the Purchaser are party to that certain Business Transfer and Subscription Agreement, dated the date hereof, (the “Business Transfer and Subscription Agreement”); unless otherwise defined herein, capitalized terms shall be used herein as defined in the Business Transfer and Subscription Agreement); and

WHEREAS, the execution and delivery of this Bill of Sale by the Sellers is required in connection with the consummation of the transactions contemplated by the Business Transfer and Subscription Agreement.

NOW, THEREFORE, in consideration of the promises and mutual agreements set forth in the Business Transfer and Subscription Agreement, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Sellers do hereby agree as follows:

Sale of Assets. The Sellers hereby sell, assign, transfer, convey and deliver to the Purchaser and its successors and assigns, forever, the entire right, title and interest of the Sellers in and to any and all of the Transferred Clinical Materials and the Transferred Tangible Assets.
Further Assurances. The Sellers hereby covenant and agree that, at any time and from time to time after the date of this Bill of Sale, at the Purchaser’s request, the Sellers will do, execute, acknowledge and deliver, or will cause to be done, executed, acknowledged and delivered, any and all further acts, conveyances, transfers, assignments, and assurances as necessary to grant, sell, convey, assign, transfer, set over to or vest in the Purchaser any of the Transferred Clinical Materials and the Transferred Tangible Assets.

Amendment. This Bill of Sale may not be amended or modified except by an instrument in writing signed by, or on behalf of, the Sellers and the Purchaser.

No Third Party Beneficiaries. This Bill of Sale shall be binding upon and inure solely to the benefit of the parties hereto and their respective successors and permitted assigns and nothing herein, express or implied, is intended to or shall confer upon any other Person any legal or equitable right, benefit or remedy of any nature whatsoever, including any rights of employment for any specified period, under or by reason of this Bill of Sale.

Severability. If any term or other provision of this Bill of Sale is invalid, illegal or incapable of being enforced by any Law or public policy, all other terms and provisions of this Bill of Sale shall nevertheless remain in full force and effect for so long as the economic or legal substance of the transactions contemplated by this Bill of Sale is not affected in any manner materially adverse to either party hereto. Upon such determination that any term or other provision is invalid, illegal or incapable of being enforced, the parties hereto shall negotiate in good faith to modify this Bill of Sale so as to effect the original intent of the parties as closely as possible in an acceptable manner in order that the transactions contemplated by this Bill of Sale are consummated as originally contemplated to the greatest extent possible.

Governing Law. This Bill of Sale and all claims or causes of action (whether at Law, in contract, in tort or otherwise) that may be based upon, arise out of or relate to this Bill of Sale or the negotiation, execution or performance hereof shall be governed by and construed in accordance with the internal Laws of the [*] applicable to agreements made and to be performed entirely within such state, without regard to the conflicts of Law principles of such state.

Counterparts. This Bill of Sale may be executed in counterparts, each of which shall be deemed an original, but all of which together shall be deemed to be one and the same agreement. A signed copy of this Bill of Sale delivered by facsimile, e-mail or other means of electronic transmission shall be deemed to have the same legal effect as delivery of an original signed copy of this Bill of Sale.

IN WITNESS WHEREOF, the Sellers have caused this Bill of Sale to be duly executed by their respective authorized officers as of the Effective Date.

ASTRAZENECA AB (PUBL)

By: ______________

Name: ______________

Title: ______________

ASTRAZENECA UK LIMITED

By: ______________

Name: ______________

Title: ______________

ASTRAZENECA PHARMACEUTICALS LP

By: ______________

Name: ______________

Title: ______________

ENTASIS THERAPEUTICS INC.
EXHIBIT 2.05(e)
ROYALTIES

1. **AZD-0914 Royalty:** The Company will pay the UK Seller and the Sweden Seller, in accordance with Section 2.05(e) of this Agreement, an amount calculated by multiplying (x) the percentage set forth under the heading “AZD-0914 Royalty” opposite the applicable amount of annual Net Sales of AZD-0914 Products set forth under the heading “Annual Net Sales of AZD-0914 Products” in the following table by (y) the applicable annual Net Sales of AZD-0914 Products:

<table>
<thead>
<tr>
<th>Annual Net Sales of AZD-0914 Products</th>
<th>AZD-0914 Royalty</th>
</tr>
</thead>
<tbody>
<tr>
<td>For that portion of annual Net Sales of AZD-0914 Products ≤ $[*]</td>
<td>Lower of [<em>]% of Net Sales or [</em>]% of any royalties received by the UK Seller</td>
</tr>
<tr>
<td>For that portion of annual Net Sales of AZD-0914 Products &gt; $[<em>] but ≤ $[</em>]</td>
<td>Lower of [<em>]% or Net Sales or [</em>]% of any royalties received by the UK Seller</td>
</tr>
<tr>
<td>For that portion of annual Net Sales of AZD-0914 Products &gt; $[*]</td>
<td>Lower of [<em>]% of Net Sales or [</em>]% of any royalties received by the UK Seller</td>
</tr>
</tbody>
</table>

2. **AZD-2514 Royalty:** The Company will pay the UK Seller and the Sweden Seller, in accordance with Section 2.05(e) of this Agreement, an amount calculated by multiplying (x) the percentage set forth under the heading “AZD-2514 Royalty” opposite the applicable amount of annual Net Sales of AZD-2514 Products set forth under the heading “Annual Net Sales of AZD-2514 Products” in the following table by (y) the applicable annual Net Sales of AZD-2514 Products:

<table>
<thead>
<tr>
<th>Annual Net Sales of AZD-2514 Products</th>
<th>AZD-2514 Royalty</th>
</tr>
</thead>
<tbody>
<tr>
<td>For that portion of annual Net Sales of AZD-2514 Products ≤ $[*]</td>
<td>[*]%</td>
</tr>
<tr>
<td>For that portion of annual Net Sales of AZD-2514 Products &gt; $[<em>] but ≤ $[</em>]</td>
<td>[*]%</td>
</tr>
<tr>
<td>For that portion of annual Net Sales of AZD-2514 Products &gt; $[*]</td>
<td>[*]%</td>
</tr>
</tbody>
</table>

3. **Calculation and Combination Products.** Annual Net Sales of a Product will be calculated by taking the sum of Net Sales of such Product for which amounts are due pursuant to during the Net Sales Based Term for all countries worldwide. In the event that a Product is sold in any country in the form of a Combination Product, Net Sales of such Combination Product shall be adjusted by multiplying actual Net Sales of such Combination Product in such country calculated pursuant to the foregoing definition of “Net Sales” by the fraction A/(A+B), where A is the average invoice price in such country of any Product that contains the same Compound(s) as such Combination Product as its sole active ingredient(s), if sold separately in such country, and B is the average invoice price in such country of each product that contains active ingredient(s) other than the Compound(s) contained in such Combination Product as its sole active ingredient(s), if sold separately in such country; provided that the invoice price in a country for each Product that contains only the Compound(s) as its sole active ingredient or a product that contains an active ingredient (other than the Product) in the Combination Product as its sole active ingredient(s) is not sold separately in a particular country, the Sellers and the Companies shall negotiate in good faith a reasonable adjustment to Net Sales in such country that takes into account the medical contribution to the Combination Product of and all other factors reasonably relevant to the relative value of, the Compound(s), on the one hand and all of the other active ingredient(s), collectively, on the other hand.

4. **Royalty Term.** On a country-by-country basis, the Company’s obligation to make royalty payments for a Product will end upon the expiration of the Net Sales Based Term for such Product in such country.

5. **Royalty Reduction.** In the event that the Company determines that rights to intellectual property owned or controlled by a third party are required to fully commercialize the Products, the Company shall have the right to negotiate and acquire such rights through a license or otherwise and to deduct from the royalty payments due to the Sweden Seller and the UK Seller [*] of the amounts paid (including milestone payments, royalties or other license fees) by the Company to such third party.
[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

AMENDMENT TO

AMENDED AND RESTATED BUSINESS TRANSFER AND SUBSCRIPTION AGREEMENT

THIS AMENDMENT TO AMENDED AND RESTATED BUSINESS TRANSFER AND SUBSCRIPTION AGREEMENT (this “Amendment”) is made and entered into as of August 28, 2017 by and among ASTRazeneca AB (PUBL), a company incorporated in Sweden under no. 556011-7482 (the “SwedEn Seller”), AstraZeneca Uk limited, a company incorporated in England under no. 3674842 (the “Uk Seller”), AstraZeneca Pharmaceuticals LP, a Delaware limited partnership (the “US Seller”), and, together with the Sweden Seller and the UK Seller, the “AZ Entities”), Entasis Therapeutics Limited, a private limited company incorporated in England and Wales (the “UK Company”), and Entasis Therapeutics Inc., a Delaware corporation and a wholly owned subsidiary of the UK Company (the “US Company”), and together with the UK Company, the “Companies”). Capitalized terms not herein defined shall have the meanings ascribed to them in the Agreement (as defined below).

RECITALS

WHEREAS, the AZ Entities and the Companies previously entered into that certain Amended and Restated Business Transfer and Subscription Agreement (the “Agreement”), dated as of March 29, 2016, and the AZ Entities and the Companies have agreed to amend the Agreement as set forth herein.

NOW, THEREFORE, in consideration of the foregoing recitals and for other consideration, the adequacy and sufficiency of which is hereby acknowledged, the parties hereto agree as follows:

SECTION 1

AMENDMENTS

1.1 Amendments to Agreement.

1.1.1 Section 2.05(d) of the Agreement is hereby amended in its entirety to read as follows:

“2.05(d):

(i) In addition, the Sweden Seller shall receive a one-time non-refundable payment of $10,000,000 (the “Milestone Payment”) upon first achievement of a First Commercial Sale (the “Milestone”). The Milestone payment shall be made within 24 months of the First Commercial Sale, and at the UK Company’s sole election, the Milestone may be paid (i) in cash by wire transfer of immediately available funds, (ii) by the issuance to the Sweden Seller of such number of Ordinary Shares as shall be equal to $10,000,000 divided by the then current fair market value of one Ordinary Share, as determined in good faith by the UK Company’s Board of Directors (the “Fair Market Value”) or (iii) a combination of cash and Ordinary Shares (valued at Fair Market Value). Notwithstanding the foregoing, if the payment of the Milestone at the time set forth above is deemed by the UK Company’s Board of Directors to be significantly burdensome to the UK Company, then the UK Company and the Sweden Seller shall explore in good faith modifying the time for the payment of the Milestone. Following the Sweden Seller’s receipt of the Milestone Payment, the Sweden Seller shall pay to the UK Seller [*] of the Milestone Payment.

Following the occurrence of the Milestone, no dividend, return of capital or other distribution shall be made by the UK Company to any shareholder until the Milestone Payment has been made in full.

(ii) In addition, the Sweden Seller is also entitled to receive a one-time non-refundable payment of $5,000,000 (the “2514 Sales Payment”) upon achievement of $[*] in cumulative Net Sales of an AZD-2514 Product (the “2514 Sales Threshold”). The 2514 Sales Payment shall be made within 3 months of the achievement of the 2514 Sales Threshold, and at the UK Company’s sole election, the 2514 Sales Payment may be paid (i) in cash by wire transfer of immediately available funds, (ii) by the issuance to the Sweden Seller of such number of Ordinary Shares as shall be equal to $5,000,000 (valued at Fair Market Value) or (iii) a combination of cash and Ordinary Shares (valued at Fair Market Value). Notwithstanding the foregoing, if at any time prior to the achievement of the 2514 Sales Threshold the fair market value of an A Preference Share of the Company as determined in good faith by the UK Company’s Board of Directors is greater than $[*] (subject to adjustment for stock splits, stock dividends, combinations, reorganizations, reclassifications, conversions or similar events affecting the A Preference Shares), the Sweden Seller shall not be entitled to the 2514 Sales Payment at such time or in the future. For the avoidance of doubt, the 2514 Sales Payment will only be waived if the Sweden Seller has the potential to liquidate or dispose on a public stock exchange the A Preference shares (all or in-part) for $[*] or more (subject to the adjustments listed above). Following the Sweden Seller’s receipt of the 2514 Sales Payment, the Sweden Seller shall pay to the UK Seller [*] of the 2514 Sales Payment. If following the occurrence of the 2514 Sales Threshold the Sweden Seller is entitled to the 2514 Sales Payment, no dividend, return of capital or other distribution shall be made by the UK Company to any shareholder until the 2514 Sales Payment has been made in full.”

1.1.2 Exhibit 2.05(e)(1) to the Agreement is hereby replaced in its entirety to read as follows:

“1. AZD-0914 Royalty: The Company will pay the UK Seller and the Sweden Seller, in accordance with Section 2.05(e) of this Agreement, an amount calculated by multiplying (x) the percentage set forth under the heading “AZD-0914 Royalty” opposite the applicable amount of annual Net Sales of AZD-0914 Products set forth under the heading “Annual Net Sales of AZD-0914 Products” in the following table by (y) the applicable annual Net Sales of AZD-0914 Products:

<table>
<thead>
<tr>
<th>Annual Net Sales of AZD-0914 Products</th>
<th>AZD-0914 Royalty %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The parties hereto have executed this Amendment as of the date first above written.

[Signature]

[Signature]

[Signature]
For that portion of annual Net Sales of AZD-0914 Products ≤ $[*]

<table>
<thead>
<tr>
<th>For that portion of annual Net Sales of AZD-0914 Products ≤ $[*]</th>
<th>Lower of [<em>]% of Net Sales or [</em>]% of any royalties received by the UK Seller</th>
</tr>
</thead>
<tbody>
<tr>
<td>For that portion of annual Net Sales of AZD-0914 Products &gt; $[<em>] but ≤ $[</em>]</td>
<td>Lower of [<em>]% of Net Sales or [</em>]% of any royalties received by the UK Seller</td>
</tr>
<tr>
<td>For that portion of annual Net Sales of AZD-0914 Products &gt; $[*]</td>
<td>Lower of [<em>]% of Net Sales or [</em>]% of any royalties received by the UK Seller</td>
</tr>
</tbody>
</table>

Notwithstanding anything contained herein, sales of an AZD-0914 Product by the Global Antibiotic Research and Development Partnership outside of the countries set forth below (as revised from time to time) shall be considered Net Sales of an AZD-0914 Product for purposes of this Agreement, but shall not be Royalty bearing. Upon written notice to the UK Seller, the UK Company shall advise the UK Seller of any changes to the list of countries set forth in this Exhibit 2.05(e)(1).

[*]

SECTION 2

MISCELLANEOUS

2.1 Entire Agreement. This Amendment and the Agreement shall constitute the entire agreement between the parties hereto pertaining to the subject matter hereof and thereof.

2.2 Severability. If any provision of this Amendment is found to be illegal or unenforceable, the other provisions shall remain effective and enforceable to the greatest extent permitted by law.

2.3 No Waiver. Other than as expressly set forth herein, this Amendment does not waive or modify any portion of the Agreement, which otherwise remain in full force and effect. No waiver of any provision of the Agreement or this Amendment is effective unless made in a writing signed by a duly authorized representative of each party.

2.4 Counterparts. This Amendment may be executed in multiple counterparts, each of which shall be considered an original, and all of which, when taken together, shall constitute one and the same document.

(Remainder of Page Intentionally Left Blank)

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

IN WITNESS WHEREOF, the parties hereto have caused this Amendment to be executed as of the day and year first above written.

EXECUTED and delivered )

as a DEED by )

ASTRAZENECA AB (PUBL) )

acting by )

a director, in the presence of: )

/s/ Per Alfredsson
Per Alfredsson
Regional Vice President
Supply EMEA

/s/ Theresia Goder
Signature of Witness
Theresia Goder
Name of Witness
DALANGSVAGE 9
Address of Witness
15168 SODERTALJE
SWEDEN

EXECUTIVE ASSISTANT
Occupation of Witness

EXECUTED and delivered )
as a DEED by

ASTRAZENECA UK LIMITED

acting by ,

a director, in the presence of:

________________________
Signature of Witness
________________________
Name of Witness
________________________
Address of Witness
________________________

Occupation of Witness

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

EXECUTED and delivered as a DEED by

ASTRAZENECA AB (PUBL)

acting by ,

a director, in the presence of:

________________________
Signature of Witness
________________________
Name of Witness
________________________
Address of Witness
________________________

Occupation of Witness

EXECUTED and delivered as a DEED by

ASTRAZENECA UK LIMITED

acting by ,

a director, in the presence of:

________________________ /s/ Alistair Collins
Signature of Witness
________________________
Name of Witness
________________________
Address of Witness
________________________

Occupation of Witness

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EXECUTED and delivered as a DEED by

ASTRAZENECA PHARMACEUTICALS LP

acting by Mariam Koohdary, in the presence of:

An Authorised Signatory

/s/ Mariam Koohdary

[s] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

EXECUTED and delivered as a DEED by

ENTASIS THERAPEUTICS LIMITED

acting by Manoussos Perros, in the presence of:

/s/ Manoussos Perros

EXECUTED and delivered as a DEED by

ENTASIS THERAPEUTICS INC.

acting by Manoussos Perros, in the presence of:

/s/ Manoussos Perros

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
69 Old Bread St.

London

Lawyer

Occupation of Witness

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
This Collaboration Agreement relating to the development, manufacture and commercialisation of zoliflodacin is entered into on the 4th day of July 2017 (the "Effective Date") by and between:

(1) Drugs for Neglected Diseases initiative ("DNDi"), a Swiss foundation with its registered office located at 15 Chemin Louis-Dunant, CH-1202 Geneva, Switzerland acting through the Global Antibiotic Research and Development Partnership ("GARDP") which is currently hosted within DNDi;

and

(2) Entasis Therapeutics Limited, a company registered in England and Wales under company number 09475809 and having its registered office at One Ashely Road, 3rd Floor, Altrincham, Cheshire WA14 2DT, United Kingdom ("Entasis")

Each a "Party" and collectively as the "Parties".

BACKGROUND:

WHEREAS, GARDP’s mission is to develop new antibiotic treatments addressing antimicrobial resistance and to promote their responsible use for optimal conservation, while ensuring equitable access for all in need;

WHEREAS, the API (as defined below) is a first-in-class drug that inhibits bacterial topoisomerase II and shows in vitro antibacterial activity against several sexually transmitted infection pathogens, including Neisseria gonorrhoeae, Chlamydia trachomatis and Mycoplasma genitalium;

WHEREAS, Entasis either owns or has been granted exclusive intellectual property rights in the API and related technology;

WHEREAS, Entasis filed an IND for the API with the United States Food and Drug Administration ("FDA") in September 2013 and has completed in the field of urogenital gonorrhoea in the United States of America a phase I single-ascending dose study and a phase I absorption, distribution, metabolism and excretion trial (the "Phase I Clinical Trials");

WHEREAS, Entasis, in collaboration with the United States National Institution of Allergies and Infectious Diseases ("NIAID") under a separate IND, has conducted a phase II study involving people with confirmed uro-genital gonococcal infection (the "Phase II Clinical Trial");

WHEREAS, the Parties wish to enter into a collaboration to further develop a drug product containing the API ("Drug Product") for the treatment of gonorrhoea caused by Neisseria gonorrhoeae, Chlamydia trachomatis and/or Mycoplasma genitalium (the "Field") including further chemistry, manufacturing and controls activities ("CMC") to be performed by DNDi, non-clinical studies to be conducted by DNDi and Entasis respectively, clinical development through a QT (TQT) study in the United States of America to be performed by Entasis in collaboration by NIAID, an international phase III multi-centre clinical trial to be sponsored by DNDi, registration of the drug product by the Parties in their respective territories, and its manufacture in order to supply and distribute the drug product in those territories on a sustainable, equitable and affordable basis; and

WHEREAS, Entasis wishes to grant to DNDi an exclusive licence to use the Entasis Background Technology (as defined below) to enable DNDi to develop the Drug Product and to register and commercialise it in certain territories, and each Party wishes to grant to the other Party certain exclusive licensing rights to use its respective Collaboration Technology (as defined below) to enable the other Party to register and commercialise the Drug Product in its territory.

NOW THEREFORE, in consideration of the mutual agreements and undertakings herein contained, the Parties agree as follows:

1. DEFINITIONS

For purposes of this Agreement (including the recitals and the Schedules), the following capitalized terms shall have the following meanings (whether used in singular or plural form):

1.1 "Affiliate" shall mean, with respect to either Party, any corporation or entity controlled by, controlling or under common control with such Party. The terms "controlling", "controlled by" or "control" shall mean: (i) the direct or indirect ownership of more than fifty percent (50%) of the voting securities of any corporation or entity, or (ii) the power to direct or cause the direction of the management or policies of such corporation or entity through the ownership of securities or interests, by contract or otherwise;

1.2 "Agreement" shall mean this Collaboration Agreement, including the recitals and the attached Schedules, as may be amended from time to time by the Parties in accordance with its terms;

1.3 "Anti-Bribery Law" shall mean any applicable law, rule, regulation, or other legally binding measure of any jurisdiction that relates to bribery or corruption;

1.4 "API" has the meaning set forth on Schedule 6;

1.5 "Background Technology" means the IP and other rights in the DNDi Background Technology or the Entasis Background Technology respectively that were either: (i) Controlled by the relevant Party as of the Effective Date; or (ii) conceived and reduced to practice, made or developed and Controlled by a Party during the Term outside the scope of the Collaboration Programme;
1.6 “Change of Control” means the occurrence of a tender offer, stock purchase, other stock acquisition, merger, consolidation, recapitalisation, reverse split, sale or transfer of assets or other transaction, as a result of which any natural or legal person gains control of an entity or a group;

1.7 “Clinical Trial” shall mean any clinical study on the Drug Product where the Drug Product is administered to humans;

1.8 “CMC” shall mean have the meaning set out in the recitals;

1.9 “Collaboration Programme” shall mean the collaboration programme to: (i) develop a Drug Product in the Field and to register such Drug Product in the Field in the DNDi Territory and the Entasis Territory in accordance with the Development Plan and the Regulatory Plan; and (ii) organise the Manufacture of such Drug Product for Commercialisation in the Field in the DNDi Territory and the Entasis Territory in accordance with the Manufacturing and Supply Plan;

1.10 “Collaboration Technology” shall mean any IP and other rights in the API, the Drug Product and the Regulatory Dossier developed or conceived and reduced to practice in the performance of the Collaboration Programme;

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1.11 “Commercialise” or “Commercialisation” shall mean any relevant activities directed to marketing, promoting, importing, distributing, offering for sale, having sold and/or selling a pharmaceutical product;

1.12 “Confidential Information” means any non-public information that is: (i) disclosed to the other Party (whether directly or indirectly) pursuant to or in the course of this Agreement howsoever disclosed that contains or relates to its Background Technology or its plans to Commercialise the Drug Product; or (ii) is generated pursuant to this Agreement by a Party including, without limitation, the respective Collaboration Technology of each Party;

1.13 “Contract Service Provider” or “CSP” shall mean any Third Party service provider contracted by either Party to perform certain aspects of the Collaboration Programme;

1.14 “Control” or “Controlled” shall mean with respect to relevant Background Technology and Collaboration Technology possession of the right, whether directly or indirectly, and whether by ownership, licence or otherwise, to assign or grant a licence, sublicense or other rights under this Agreement without violating the terms of any agreement or other arrangement with any Third Party;

1.15 “Data Room” shall have the meaning set out in Clause 7.11;

1.16 “Development Plan” shall mean a development plan outlining the non-clinical and clinical development plans and CMC plans for the Drug Product to meet the criteria of the TPP, which Development Plan is attached as Schedule 1 hereto, as amended from time to time in accordance with the terms of this Agreement;

1.17 “DNDi Background Technology” shall mean any Background Technology of DNDi that is necessary or useful for the performance of the Collaboration Programme;

1.18 “DNDi Collaboration Technology” shall mean: (i) [*]; and; (ii) [*]; and (iii) all other Collaboration Technology that is developed or conceived by DNDi (or its employees, Sublicensees or agents, including CSPs) in the performance of the Collaboration Programme;

1.19 “DNDi Indemnified Parties” shall have the meaning set out in Clause 11.1;

1.20 “DNDi Territory” means all those countries and regions listed as being in DNDi’s Territory as described in Schedule 2;

1.21 “Drug Product” shall have the meaning set out in the recitals;

1.22 “Drug Regulatory Authority” shall mean any competent authority in any country of the Territory with authority over the Drug Product and/or a Clinical Trial including, without limitation, the FDA and the EMA;

1.23 “Effective Date” shall mean the date set forth at the head of this Agreement;

1.24 “EMA” shall mean the European Medicines Agency;

1.25 “Enforcing Party” shall have the meaning set out in Clause 7.19;

1.26 “Entasis Background Technology” shall mean any Background Technology of Entasis relating to the API that is necessary or useful for the performance of the Collaboration Programme; provided, however, that if any Third Party becomes an Affiliate of Entasis after the Effective Date, Entasis Background Technology shall exclude any IP controlled by such Third Party before such Third Party became Entasis’s Affiliate;

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1.27 “Entasis Collaboration Technology” shall mean any Collaboration Technology that is developed or conceived by Entasis (or its employees, Sublicensees or agents, including CSPs) in the performance of the Collaboration Programme;

1.28 “Entasis Indemnified Parties” shall have the meaning set out in Clause 11.2;

1.29 “Entasis Patents” shall mean Patent Rights included in the Entasis Background Technology as of the Effective Date as described in Schedule 3;

1.30 “Entasis Territory” means all those all those countries listed as being in Entasis’ Territory as described in Schedule 2;

1.31 “FDA” shall mean the meaning set out in the recitals;

1.32 “Field” shall have the meaning set out in the recitals;

1.33 “Filing Party” shall have the meaning set out in Clause 5.8;

1.34 “Force Majeure” shall mean an event which is (i) unpredictable, (ii) unavoidable and (iii) outside of the reasonable control of a Party or its CSP that prevents or substantially interferes with the performance by such Party of any of its obligations under this Agreement;

1.35 “Future Indications” shall mean any community-acquired indications outside of the Field;

1.36 “Future Indications Technology” shall have the meaning set out in Clause 7.10;

1.37 “Good Clinical Practice” shall mean the guideline of the ICH Harmonized Tripartite Guidelines: Guidelines for Good Clinical Practice E6 (R1) of 10 June 1996 (as amended from time to time), being an international ethical and scientific quality standard for designing, conducting, recording, and reporting Clinical Trials that involve the participation of human subjects;

1.38 “Good Manufacturing Practices” or “GMP” shall mean regulations and published guidelines related to current good manufacturing practices that relate to the testing, manufacturing, processing, packaging, holding or distribution of drug or biologic drug substances and finished drugs or biologics as set forth in the EU GMP Guide on good manufacturing practices for medicinal products for human use laid down in Commission Directives 91/356/EEC, as amended by Directive 2003/94/EC, and 91/412/EEC respectively, as amended during the Term of this Agreement;

1.39 “Granule Formulation” means a formulation of the API that has been developed by Entasis using granules containing amorphous drug substance in a water-dispersable sachet;

1.40 “Holding Point” shall have the meaning set out in Clause 4.4;

1.41 “ICH” shall mean the International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use;

1.42 “IND” shall mean an investigational new drug application, clinical trial authorization or equivalent application filed with the applicable Drug Regulatory Authority, which application is required to commence human clinical trials in the applicable country;

1.43 “Indemnification Claim Notice”; “Indemnified Party”, and “Indemnifying Party” shall each have the meaning set out in Clause 11.3;

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

1.44 “Know How” means technical and other information which is not in the public domain including information relating to: (i) non-clinical data including pharmacological, toxicological and metabolic data and results of any non-clinical studies relevant to the API and the Drug Product; (ii) clinical safety and efficacy data including data analyses, study reports and information contained in protocols, filings or other submissions to or responses from ethical committees and Drug Regulatory Authorities; (iii) pharmacovigilance data; (iv) production processes including any drug master file, specifications, techniques, manufacturing line procedures, CMC data, SOPs, quality analysis and quality control processes and techniques and other documentation retained to comply with GMP; and (v) any relevant information relating to product supply chain of the Drug Product including the API, fill, finish and primary and secondary items. Know How includes: (a) documents containing Know How; and (ii) any legal rights including trade secrets, copyright, database or design rights protecting such Know How;

1.45 “Infringement Notice” shall have the meaning set out in Clause 7.19;

1.46 “Intellectual Property” or “IP” shall mean Patent Rights, Know How, copyrights, any improvements, enhancements or modifications to any of the foregoing and any rights or property similar to any of the foregoing in any part of the world, whether registered or not;

1.47 “Joint Steering Committee” or “JSC” shall mean the joint steering committee having the role specified in Clause 8.

1.48 “Losses” shall mean any and all losses, damages, liabilities, costs and expenses (including without limitation reasonable legal fees and expenses) taking account of the duty on the Party suffering such Losses to mitigate such Losses;

1.49 “Manufacturing” shall mean all activities relating to making/or having made the API and/or the Drug Product and all associated activities including labelling/or having labelled, and packaging or having packaged the Drug Product in accordance with GMP;
“Manufacturing and Supply Plan” shall mean the plan for manufacture of the API and the Drug Product and its supply to the DNDi Territory and to the Entasis Territory to be developed and by the Parties in accordance with Clause 6;

“Marketing Authorisation” shall mean all approval(s), registration(s) and authorisation(s) necessary to be obtained from an applicable Drug Regulatory Authority to lawfully import, promote, distribute and sell the Product in the Field in a country of the DNDi Territory or the Entasis Territory, as applicable;

“NIAID” shall have the meaning set out in the recitals;

“Non-Filing Party” shall have the meaning set out in Clause 5.8;

“Patent Rights” shall mean any: (i) patents and patent applications (provisional and non-provisional); (ii) continuations, divisionals, continuations-in-part, continued examinations, re-examinations, reissues, utility models, petty and other patent applications claiming subject matter therein or claiming priority from any of the foregoing, and all patents that issue there from; (iii) counterparts, substitutions, restorations, extensions (including, without limitation, patent term extensions), supplementary protection certificates, registrations, confirmations, validations and renewals of any of the foregoing; and (iv) invention certificates and other government grants for the protection of inventions or industrial designs;

“Pharmacovigilance Agreement” shall have the meaning set out in Clause 9.2;

“Phase I Clinical Trials” shall have the meaning set out in the recitals;

“Phase II Clinical Trial” shall have the meaning set out in the recitals;

“Phase III MC Trial” shall mean an international phase III multi-centre Clinical Trial to be conducted consistent with the Development Plan with the objective of demonstrating the safety and efficacy of the Drug Product in people infected with Neisseiria gonorrhoeae.

“Phase IV Clinical Trial” shall mean any Clinical Trial conducted after the first Marketing Authorisation for the Drug Product has been obtained;

“Project Leader” shall have the meaning set out in Clause 8.2;

“Promotional Materials” shall mean promotional, advertising, communication and educational materials relating to the Drug Product for use in connection with the marketing, promotion and sale of the Drug Product and includes promotional literature, product support materials and promotional giveaways;

“QT (TQT) Study” shall mean a study aimed at investigating the API liability to prolong the QT interval (incorporating a bioavailability study) to be performed on the Granule Formulation by Entasis in collaboration with NIAID prior to commencement of the Phase III MC Trial;

“Regulatory Dossier” means all regulatory documents and filings registered with a Drug Regulatory Authority for a Marketing Authorisation containing the administrative, safety, efficacy, quality, non-clinical and clinical data and CMC data for the Drug Product as it may change from time to time;

“Regulatory Plan” shall mean a regulatory plan outlining the regulatory strategy for obtaining Marketing Authorisations for the Drug Product and split of regulatory responsibilities of the Parties with the aim of ensuring equitable and affordable access to the Product for people in the DNDi Territory and the Entasis Territory at the earliest possible date, as further described in Schedule 4 hereto and in Clause 5, as may be amended from time to time;

“Standard Operating Procedure” or “SOP” shall mean detailed, written instructions to achieve uniformity of the performance of a specific function, adopted within the organisation of each of the Parties;

“Sublicensor” shall mean a Third Party appointed by either Entasis or DNDi or an Affiliate of Entasis or DNDi (other than a CSP) to carry out Manufacturing and/or Commercialisation of the Drug Product in its Territory or a part thereof;

“Target Product Profile” or “TPP” shall mean the set of potential characteristics and attributes for the Drug Product, described in Schedule 5 hereto, and revised from time to time by mutual consent through the JSC;

“Term” shall mean the period commencing after the Effective Date and unless terminated earlier in accordance with the terms of this Agreement, expiring country by country of the DNDi Territory and the Entasis Territory until the longer of: (i) the expiry of any Patent Rights in such country; or (ii) ten years from the first Marketing Authorisation for such Drug Product for the Field in such country.

“Territory” shall mean the DNDi Territory and/or the Entasis Territory as the context requires;

“Third Party” shall mean any person, organization or entity other than the Parties and their Affiliates;

“Third Party Claim” shall have the meaning set out in Clause 11.3.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
2. **OBJECTIVE OF THIS AGREEMENT**

2.1 The objective of this Agreement is to set forth:

2.1.1 the principles of the collaboration between DNDi and Entasis in the performance of the Collaboration Programme;

2.1.2 the obligations and roles and responsibilities of the Parties with respect to performance of the Collaboration Programme;

2.1.3 the conditions pursuant to which DNDi shall provide to Entasis the right to use the DNDi Background Technology and Entasis shall provide to DNDi the right to use the Entasis Background Technology; and

2.1.4 licensing and rights to use the Collaboration Technology.

3. **COLLABORATION PROGRAMME**

3.1 Except to the extent otherwise specified in any specific clause of this Agreement, each Party shall use commercially reasonable endeavours to perform its roles and activities within the Collaboration Programme and in a timely manner.

3.2 Each Party may enlist the services of any CSP to perform its duties under the Collaboration Programme. The Party engaging a CSP shall ensure that the CSP allocates sufficient time, effort, equipment and facilities to the Collaboration Programme and utilizes personnel with sufficient skills and experience as are required to satisfy the requirements of the Collaboration Programme.

3.3 In the performance of its obligations in relation to the Collaboration Programme each Party shall comply with its own SOPs, all applicable laws and regulations (including but not limited to Good Clinical Practice, Good Manufacturing Practices and ICH guidelines and national regulatory requirements and codes of practice and ethics committee or similar approvals) and shall obtain all applicable approvals and licences that may be required in order for it to perform its activities.

3.4 Except as otherwise expressly set out in this Agreement, each Party shall bear any and all costs that are incurred by it in connection with any activity for which such Party is responsible pursuant to this Agreement. Each Party shall have the right, in consultation with the other Party, to seek financing from funding agencies for any part of the Collaboration Programme, provided always that the Party obtaining such funding continues to comply with its obligations hereunder and that obtaining such funding does not lead to any conflict or restriction with respect thereto.

4. **DEVELOPMENT OF THE DRUG PRODUCT**

4.1 The Parties shall use commercially reasonable endeavours to develop the Drug Product in the Field in accordance with this Clause 4, the Development Plan and the Regulatory Plan.

4.2 Each Party in the performance of its activities in relation to the Development Plan will reasonably consider the views of the other Party.

4.3 The Party conducting a study (e.g., Entasis for the QT (TQT) Study and DNDi for the Phase III MC Trial as per below) or pharmaceutical development shall make appropriate updates to the investigator’s brochure as required by Drug Regulatory Authorities and/or ethics committees, and the other Party shall reasonably co-operate with the first Party.

4.4 At each decision point specified set out in the Development Plan (a “Holding Point”), the Parties shall determine through the JSC whether development of the Drug Product should continue beyond the Holding Point and if so, whether changes to the Development Plan are required prior to commencement with the remainder of the activities set out in the Development Plan.

**QT (TQT) Study**

4.5 The Development Plan envisages that clinical development activities will commence with a QT (TQT) Study on the Granule Formulation in the United States of America. Entasis shall use commercially reasonable endeavors perform and fund the QT (TQT) Study in collaboration with NIAID (including procuring samples of the Granule Formulation for the QT (TQT) Study).

4.6 Entasis shall:

4.6.1 regularly update DNDi of status of the QT (TQT) Study and in particular shall notify DNDi promptly of any serious adverse events and any communications with or inspections by the Drug Regulatory Authority; and

4.6.2 promptly provide to DNDi once finalized and validated by Entasis with NIAID the results of the TQ (TQT) Study including without limitation clinical study reports.

**Phase III MC Trial**
4.8 DNDi shall use commercially reasonable endeavours to perform and fund the Phase III MC Trial including:

4.8.1 select the centres at which the Phase III MC Trial will be conducted;

4.8.2 submit an IND and the regulatory clinical trial application(s) for the Phase III MC Trial to the FDA, EMA, and other applicable Drug Regulatory Authorities;

4.8.3 arrange with a CSP for the Drug Product manufacturing that is required for the Phase III MC Clinical Trial;

4.8.4 regularly update Entasis through the JSC about the regulatory status of clinical trial applications and the status of the Phase III MC Trial; and

4.8.5 promptly provide to Entasis once finalized and validated by DNDi the results of the Phase III MC Trial including without limitation clinical study reports.

Entasis shall co-operate with DNDi in DNDi’s performance of the Phase III MC Trial including, without limitation, by:

4.9.1 providing DNDi with all Know How relating to the API and the Drug Product that is necessary for DNDi to perform its obligations; and

4.9.2 assisting DNDi to develop a robust protocol for the Phase III MC Trial and committing reasonably sufficient time and resources to do so.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

Pharmaceutical Development

4.10 Pharmaceutical development of the Drug Product will commence as set out in the Development Plan in order to explore alternative formulations of the Drug Product used in the Phase III MC Trial.

4.11 DNDi shall use reasonable endeavours to perform and finance the CMC activities (as detailed in the Development Plan) in accordance with the Development Plan. Entasis shall provide all Know How relating to the API that DNDi requires including the Granule Formulation.

4.12 DNDi shall be responsible for organising the manufacture and supply of the Drug Product for the Phase III MC Trial and selecting its CSP for this purpose.

4.13 DNDi shall have title to all batches of the Drug Product produced in the course of the Development Plan and may use such Drug Product for the purpose of any Clinical Trial that it performs or for Commercialisation in the DNDi Territory. Should it be impracticable for DNDi to use such batches prior to expiration, the Parties will collaborate to identify different ways to use such batches, which options may include, if agreed by the Parties at such time, the purchase by Entasis of batches of the Drug Product for use in the Entasis Territory at fair market value.

Future Indications

4.14 In order to preserve efficacy and responsible use of the Drug Product, each Party agrees that neither the API nor the Drug Product shall be developed by or on behalf of either Party for the Future Indications without the prior consent of the other Party, not to be unreasonably withheld.

Further Development Responsibilities

4.15 If a Party desires to conduct a Clinical Trial in the Territory of the other Party, then such Party shall (i) provide the other Party with a copy of the proposed protocol of such Clinical Trial for review and comment by the other Party, which such comments shall be considered by the first Party in good faith, and (ii) obtain the consent of the other Party, such consent not to be unreasonably withheld.

4.16 Each Party shall keep or cause to be kept written laboratory notebooks and other records and reports of the progress of the Development Plan and its activities in sufficient detail and in good scientific manner. Such notebooks and other records must properly reflect all work done in relation to the Development Plan and the results achieved.

4.17 Should any animals be involved in any aspect of the Development Plan each Party will treat such animals with humane care and shall adhere to the following core animal welfare principles: (a) animals must be provided a physical environment that is consistent with their physiological and behavioral needs; (b) animals must be provided potable water and a diet that meets their nutritional requirements; (c) animals must be provided a basic standard of medical care for all health issues, including those related to research, which is consistent with current veterinary medical standards; (d) efforts should be made to avoid, or when this is not possible, to minimize each animal’s pain, discomfort and distress. Anesthetics and analgesics should be used wherever necessary and feasible; (e) attending veterinarians must be provided the necessary resources and have the authority to manage animal welfare issues and to minimize pain and distress; (f) individuals responsible for the care and use of laboratory animals must be adequately trained in current standards of care and ethical treatment of laboratory animals and competency in planned animal procedures should be assessed prior to working with the animals; (g) whenever possible, the 3Rs of refinement, reduction and replacement will be adopted if compatible with the objectives of the study design; (h) when necessary, animals must be provided a humane death using techniques that are consistent with current veterinary medical standards when predetermined endpoints have been achieved or when pain or distress cannot otherwise be alleviated.
5. **REGULATORY STRATEGY AND ACTIVITIES FOR OBTAINING MARKETING AUTHORIZATION**

5.1 The regulatory strategy (including timelines and milestones) and the regulatory responsibilities of the Parties are set out in detail in the Regulatory Plan. As of the Effective Date the regulatory strategy is based on the principles that:

5.1.1 clinical development is intended to facilitate the process for registration of the Drug Product in the first instance with the FDA and the EMA;

5.1.2 Entasis shall use its best efforts to file the application for the first Marketing Authorisation for the Drug Product in the Field with the FDA, provided that, in Entasis’ reasonable determination, the data generated by completion of the Phase III MC Trial will be acceptable by the FDA, and would not otherwise cause Entasis to violate applicable law; and

5.1.3 Entasis is responsible for obtaining Marketing Authorisations for the Drug Product in the Entasis Territory if and as it elects, and DNDi is responsible for obtaining Marketing Authorisations for the Drug Product in such countries of the DNDi Territory as it elects.

**First Marketing Authorisation with the FDA and the EMA**

5.2 Entasis shall:

5.2.1 use its best efforts to file the application for the first Marketing Authorisation for the Drug Product in the Field with the FDA by no later than six (6) months from the completion of the Phase III MC Trial (which shall mean database lock for clean file for the Phase III MC Trial) provided that, in Entasis’s reasonable determination, the data generated by completion of the Phase III MC Trial will be acceptable by the FDA, and would not otherwise cause Entasis to violate applicable law;

5.2.2 use commercially reasonable endeavors to maintain the Marketing Authorisation with the FDA when granted;

5.2.3 use commercially reasonable endeavors to file the application for the first Marketing Authorisation for the Drug Product in the Field with the EMA;

5.2.4 use commercially reasonable endeavors to reasonably support DNDi in its conduct of any additional activities conducted by DNDi pursuant to Clause 5.3.2;

5.2.5 permit DNDi to review and make suggestions in relation to the Regulatory Dossier prior to submission to the FDA and EMA and reasonably consider such suggestions;

5.2.6 inform DNDi regularly through the JSC of the progress of the regulatory activities for obtaining Marketing Authorization with the FDA and the EMA; and

5.2.7 promptly provide to DNDi a copy of the Regulatory Dossier file submitted to the FDA and the EMA and any correspondence in relation thereto.

5.3 DNDi shall:

5.3.1 provide to Entasis relevant clinical and CMC data in its possession that is required for the purpose of registering the Drug Product with the FDA and the EMA, and, upon reasonable request by Entasis, DNDi shall reasonably assist Entasis in the preparation of regulatory materials for the FDA and the EMA registration, including the applicable portion of the CMC section;

5.3.2 use commercially reasonable endeavors to conduct any additional activities that may be required by the FDA or be agreed between the Parties in addition to those set forth in the Development Plan to obtain the FDA Marketing Authorization;

5.3.3 be responsible for the full costs of the additional activities mentioned under clause 5.3.2 to obtain the FDA Marketing Authorization;

5.3.4 review and make suggestions in relation to the Regulatory Dossier prior to submission by Entasis to the FDA and the EMA; and

5.3.5 reimburse Entasis for *[* of costs incurred by Entasis in filing the Marketing Authorisation for the Drug Product in the Field with the EMA if DNDi uses or references such Marketing Authorisation in any filing for Marketing Authorisation in the DNDi Territory in accordance with Clause 5.7 within [* of DNDi submitting any such Marketing Authorisation in the DNDi Territory.

**Phase IV Clinical Trials**
5.4 Each Party shall be responsible for financing such additional Clinical Trials in its respective Territory as it elects to conduct in accordance with this Agreement.

Market Authorizations in countries other than the USA

5.5 Each Party will, except as otherwise specified in this Agreement, be responsible at its own cost, for using commercially reasonable endeavours to take all other necessary steps for obtaining and, during the Term of this Agreement, maintaining Marketing Authorisations in its Territory on behalf of itself or its Sublicensee if appropriate.

5.6 Each Party shall use commercially reasonable endeavours to assist the other Party (and where appropriate its Sublicensee), at the other Party’s cost, to register the Drug Product for use in the Field in its Territory in accordance with the Regulatory Plan, and to answer questions from any Drug Regulatory Authority with respect to the API and the Drug Product.

Use of Regulatory Dossier and References

5.7 Each Party (and where appropriate its Sublicensees) shall be entitled, without the approval or consent of the other Party, to have full access to the Regulatory Dossier submitted to the FDA and the EMA by Entasis, to use it with any Drug Regulatory Authority in its Territory and to exercise its licensing rights (including sublicensing rights in accordance with this Agreement).

5.8 The Party submitting a filing to a Drug Regulatory Authority (the “Filing Party”) shall have discretion to decide the documents (or extracts thereof) which will be included in the particular Regulatory Dossier that it submits and to modify and translate such documents as required. Promptly after such submission, the Filing Party shall notify the other Party (the “Non-Filing Party”) that such regulatory filing has been made, and upon the request of the Non-Filing Party, provide it with a copy of each such submission. Each Party shall update the other Party as to the status of each Regulatory Dossier within the different countries where it is submitted in its Territory, and will provide the other Party through the JSC with a report on its exchanges with the applicable Drug Regulatory Authority.

5.9 The Filing Party shall provide to the Non-Filing Party (and use commercially reasonable endeavours to procure that its Sublicensees provide) in writing letters of reference, granting the Non-Filing Party

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
6.1.1 the Parties shall develop a detailed forecasting, supply, access and implementation plan for the supply of the Drug Product and define related operational supply chain management processes to ensure availability and access of the Drug Product in the Field with the consultation, as appropriate, of one or more funding agencies or partners, e.g., the World Health Organisation;

6.1.2 the Parties will use commercially reasonable endeavours to optimize production costs and will seek opportunities to jointly appoint Manufacturing Sublicensee(s) where possible;

6.1.3 the Parties will give due consideration to the need to ensure continued efficacy and responsible use of the Drug Product and will therefore seek to minimize the number of Sublicensees for Manufacturing;

6.1.4 if the appointment of joint Manufacturing Sublicensee(s) is not possible, each Party will have the right to Manufacture the Drug Product anywhere in the world (and subject to Clauses 7.6 and 7.8 appoint a Sublicensee to do so) and to Commercialise the Drug Product in the countries in its respective Territory for which a Marketing Authorization has been obtained;

6.1.5 each Party shall make reasonably available to nominated representatives of the other Party appropriate personnel to educate and train such representatives in relation to Know How that may be required to Manufacture the Drug Product;

6.1.6 each Party will ensure that any Drug Product is supplied with appropriate instructions for use and neither Party will promote the Drug Product for any use or indication other than those specified in the Marketing Authorisation in the Territory or part thereof from time to time or make any medical or promotional claims regarding the Drug Product other than permitted by law;

6.1.7 each Party will use commercially reasonable endeavours to ensure that the Drug Product is made available at price which is affordable and sustainable in its respective Territory and any part thereof;

6.1.8 the Drug Product manufactured for Commercialisation in the Entasis Territory shall be reasonably distinguished from the Drug Product for Commercialisation in the DNDi Territory, as agreed by Parties;

6.1.9 unless otherwise agreed each Party will be responsible for packaging and labelling of Drug Products in its Territory;

6.1.10 each Party shall be responsible for its own Promotional Materials for use in its Territory and for filing such Promotional Materials with the relevant Drug Regulatory Authority as required;

6.1.11 each Party (or its Sublicensee) shall use its own name and/or logo for Commercialisation in its Territory unless otherwise agreed.

6.2 DNDi will promptly notify Entasis in accordance with the Development Plan if DNDi, either itself or through an Affiliate or a Third Party on its behalf, improves, modifies, or enhances the formulation of the Drug Product;

6.3 It is acknowledged that Entasis has certain obligations to make milestone payments to Astra Zeneca AB (and/or its affiliates) in relation to the API (“Astra Zeneca”). The Parties agree that any such payments to Astra Zeneca will be paid in full by Entasis and that such costs shall not be transferred to DNDi (and/or any of its Sublicensee(s)) whether directly or indirectly or applied to the costs of any supply of Drug Product for Commercialisation in the DNDi Territory.

7. INTELLECTUAL PROPERTY

Ownership

7.1 All rights in, title to and interest in the DNDi Background Technology and the DNDi Collaboration Technology shall be owned by DNDi. DNDi shall promptly notify Entasis upon the creation of DNDi Background Technology and DNDi Collaboration Technology. Notwithstanding the foregoing or Clause 7.17, DNDi shall solely own all rights, title, and interest in and to all IP developed or conceived and reduced to practice in DNDi’s performance of [*] as DNDi Collaboration Technology; provided, that if DNDi does not file for Patent Rights on DNDi Collaboration Technology that would be reasonably patentable in the DNDi Territory or Entasis Territory within six (6) months of making such invention, or thereafter does not use commercially reasonable endeavors to prosecute and maintain such Patent Rights, then DNDi shall and hereby does assign to Entasis all of DNDi’s right, title, and interest in and to such IP. DNDi shall take, and shall cause its employees, agents, sublicensees, and contractors to take, all further acts reasonable required to effectuate the transfer of such IP. Any IP transferred to Entasis pursuant to this Clause 7.1 shall thereafter be considered as Entasis Collaboration Technology.

7.2 All rights in, title to and interest in the Entasis Background Technology and the Entasis Collaboration Technology shall be owned by Entasis. Entasis shall promptly notify DNDi upon the creation of Entasis Background Technology and Entasis Collaboration Technology.
7.3 The Parties agree that each Party shall retain ownership of all rights, title and interest in any part of the Regulatory Dossier which it (or any Party acting on its behalf) has authored provided that each Party shall be entitled to use the Regulatory Dossier for the purposes set out in Clauses 5.7 to 5.9 inclusive without the approval of the other Party.

7.4 Each Party shall procure that under the terms of any appointment of a CSP or Sublicensee that the CSP or Sublicensee does all such acts and things necessary to vest all right, title and interest in its Collaboration Technology in such Party.

Licensing

7.5 Entasis hereby grants to DNDi, a worldwide, fully paid up, exclusive and royalty-free license with the right to sublicense to any Sublicensee (subject to Clause 7.6) through multiple tiers to use the Entasis Background Technology and the Entasis Collaboration Technology:

7.5.1 in connection with all activities associated with the development of the Drug Product in the Field in accordance with the Development Plan and the Regulatory Plan;

7.5.2 to Manufacture the API and the Drug Product for Commercialisation in the Field in the DNDi Territory; and

7.5.3 to register and obtain and maintain Marketing Authorisation in the DNDi Territory and to Commercialise the Drug Product in the Field in the DNDi Territory.

For the avoidance of doubt, subject always to Clause 4.14, Entasis retains the right to use and grant licenses to the Entasis Background Technology and the Entasis Collaboration Technology (i) to perform its obligations under this Agreement and (ii) for any purposes not set out above.

7.6 The appointment of distributors and other commercial Sublicensees (for clarity, excluding all CSPs) by DNDi will be subject to Entasis’ prior written consent, not to be unreasonably withheld or delayed, provided that the Sublicensee is required to comply with the restrictions set out in sub-clauses Clause 7.5.1 to 7.5.3 inclusive.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
7.14 Entasis shall be responsible for maintaining the Data Room for a period of one (1) year following expiry or termination of this Agreement and shall permit nominated representatives of DNDi or any DNDi CSP or Sublicensee to have access to the data room during that period.

**Filing, prosecution and maintenance and infringement**

7.15 Entasis shall use its best efforts to file, prosecute, and maintain the Patent Rights claiming the Entasis Background Technology or the Entasis Collaboration Technology in all countries in the DNDi Territory listed on Schedule 3 as of the Effective Date and in any country in Schedule 3 in the DNDi Territory or the Entasis Territory in which Manufacturing is agreed to take place in accordance with the Manufacturing and Supply Plan.

7.16 Entasis shall notify DNDi (i) within ten (10) business days for any material updates, and (ii) every six (6) months for non-material changes with regard to all filings made for Patent Rights in the DNDi Territory including sending DNDi a copy of any such filing and otherwise shall keep DNDi informed of all material developments in relation to such Patent Rights and shall promptly provide DNDi with copies of relevant documents related to the filing, prosecution and maintenance of such Patent Rights. Entasis shall consider in good faith any reasonable comments made by DNDi in relation to the prosecution of Patent Rights in the DNDi Territory when making any submission to a Patent Rights office and in the conduct of any proceedings in relation to such Patent Rights. DNDi shall reimburse Entasis for costs and expenses for the maintenance of such Patent Rights in the DNDi Territory.

7.17 DNDi shall have the right but not the obligation to file, prosecute, and maintain the Patent Rights claiming the DNDi Background Technology and the DNDi Collaboration Technology on a world-wide basis (including for the avoidance of doubt in the Entasis Territory and the DNDi Territory).

7.18 DNDi shall keep Entasis promptly informed of all filings made for Patent Rights in the Entasis Territory including sending Entasis a copy of any such filing and otherwise shall keep Entasis informed of all material developments in relation to such Patent Rights and shall promptly provide Entasis with copies of relevant documents related to the filing, prosecution and maintenance of such Patent Rights. DNDi shall consider in good faith any reasonable comments made by Entasis in relation to the prosecution of Patent Rights in the Entasis Territory when making any submission to a Patent Rights office and in the conduct of any proceedings in relation to such Patent Rights. In the event that DNDi declines to file prosecute, maintain or defend any pending Patent Rights in any country of the Entasis Territory or the DNDi Territory it shall notify Entasis in writing of such decision and within thirty (30) days and Entasis and/or its Sublicensee shall have the right (but not the obligation) to file, prosecute and maintain such Patent Rights in the Entasis Territory or the DNDi Territory at Entasis’ costs and expense. DNDi shall execute any documents to transfer control of such filing and maintenance to Entasis.

7.19 If a Party becomes aware of any actual, threatened or suspected infringement or misuse by a Third Party of any Patent Rights belonging to the other, it shall promptly notify the other Party in writing of all available evidence and details available to it (the “Infringement Notice”). The Party in whose Territory the infringement is occurring (i.e., DNDi in the DNDi Territory and Entasis in the Entasis Territory) (the “Enforcing Party”) will discuss the matter with the other Party to solicit its views as to any action that may or not be taken in relation thereto. The Enforcing Party shall have the sole right, but not the obligation to bring, defend, or maintain and control any suit or action against any actual, threatened or suspected infringement. The Enforcing Party will bear the relevant expenses, but the other Party shall reasonably assist and cooperate with the Enforcing Party in any enforcement or defence at the Enforcing Party’s cost. If the other Party or its Sublicensee is required to join the Enforcing Party in such suit or action in order to enforce such Patent Rights, the other Party shall use commercially reasonable endeavors to execute all papers and perform all other acts as may be reasonably required at the cost of the Enforcing Party. If the Enforcing Party (or its Affiliate) lacks standing to bring any such action due to lack of ownership, it may ask the owning Party or its Sublicensee to do so at the Enforcing Party’s cost and in which case the owning Party or its Sublicensee will conduct such action in accordance with the Enforcing Party’s instructions. In any infringement proceedings, the Enforcing Party shall retain all costs and damages recovered, whether ordered or as part of a settlement.

7.20 If DNDi is the Enforcing Party and fails to take proceedings for more than six (6) months after having been alerted to the infringement, Entasis may give notice to DNDi demanding that DNDi take such proceedings within thirty (30) days of the date of the notice and, if DNDi does not do so, Entasis shall be entitled to take over such proceedings at its own cost and expense in which case DNDi shall transfer to Entasis the conduct of any claim or proceedings, including any counterclaim for invalidity or unenforceability or any declaratory judgment action. DNDi shall provide all necessary assistance to Entasis in relation to such proceedings at Entasis’ cost. Entasis shall have the sole right to settle such proceedings including any counterclaim for invalidity or unenforceability. If Entasis succeeds in such proceedings, for any amounts attributable to lost sales of Drug Product in the DNDi Territory, such amounts will be distributed to DNDi and any other amounts will be retained by Entasis.

7.21 In the event of any Third Party challenge to the validity of any Patent Rights, the Enforcing Party shall have the sole right to decide upon and to implement the course of action with respect to such challenge (including but not limited to, the decision to defend, not to defend or settle such challenge) at its own cost or expense and the other Party shall reasonably assist in any defence at the cost of the Enforcing Party (including, without limitation the provision of information and expertise relating to the relevant Patent Rights). Notwithstanding the foregoing, if DNDi is the Enforcing Party and fails to take action within six (6) months after having been alerted to the Third Party challenge to the validity of DNDi’s Patent Rights, Entasis may give notice to DNDi demanding that DNDi take such action within thirty (30) days of the date of the notice and, if DNDi does not do so, Entasis shall be entitled to take such actions at its own cost and expense in which case DNDi shall transfer to Entasis the conduct of any actions. DNDi shall provide all necessary assistance to Entasis in relation to such actions at Entasis’s cost. Entasis shall have the sole right to settle such
7.22 If either Party receives a formal notice from a Third Party that the development, Manufacture or Commercialisation of the Drug Product in its Territory under this Agreement infringes or otherwise violates the intellectual property rights of such Third Party in its Territory or a part thereof, then such Party must promptly notify the other Party in writing of such allegation. As soon as reasonably practicable after the receipt of such notice, the Parties will meet and consider the course of appropriate action with respect to such allegation of infringement. In such instance, each Party will, have the right to defend any action naming it; however, at all times the Parties will cooperate, share all material notices and filings in a timely manner, provide all reasonable assistance to each other and use good faith efforts to mutually agree upon an appropriate course of action, including, as appropriate, the preparation of material court filings and any discussions concerning a potential defence and/or settlement of any such claim. The rights and obligations set out in this paragraph will apply even if only one Party defends any such claimed infringement action commenced by a Third Party. A non-owning Party will not enter into any settlement of such proceedings without the owning Party’s prior consent, not to be unreasonably withheld or delayed.

7.23 The Parties agree to use commercially reasonable endeavors to cooperate in an effort to avoid loss of Patent Rights related to the Drug Product including by executing any documents as may be reasonably required.

8. GOVERNANCE AND PROJECT MANAGEMENT

8.1 Within thirty (30) days from the Effective Date, the Parties shall establish and run a JSC to oversee the Collaboration Programme and which will be responsible for ensuring strategic coordination and exchange of information between the Parties.

8.2 Each Party shall further appoint a project leader for the Collaboration Programme (each, a “Project Leader”). Each Party may replace its Project Leader from time to time by giving a written notice to the other Party (including by email) as soon as reasonably practicable following such change. Each Project Leader shall be the primary point of contact for the Collaboration Programme for that Party.

8.3 The JSC shall be composed of six (6) representatives. Each Party shall be entitled to appoint three (3) representatives to the JSC (one of whom must be the Project Leader). JSC representatives must be appropriate for the primary function of the JSC in terms of their seniority, availability and function in their respective organisations, training and experience. The chairperson of the JSC will alternate between the Project Leader of DNDi and the Project Leader of Entasis at each JSC meeting.

8.4 Each Party shall be entitled to change its JSC representatives and will notify the other of any change. Each Party shall use reasonable efforts to keep an appropriate level of continuity in representation. JSC representatives may be represented by another person designated in writing (which shall include email) by the absent JSC representative.

8.5 The JSC shall hold meetings in person or by teleconference or videoconference as frequently as members of the JSC may agree shall be necessary, but no less frequently than (4) times per year. The chairperson shall be responsible for organising the JSC meeting, the first of which shall be held within thirty (30) days after the Effective Date at the premises of DNDi. Special meetings of the JSC may be called by any JSC member on written request to the then current chairperson of the JSC. Each Party shall provide the agenda items and written copies of associated materials that it wishes to be considered no later than seven (7) days prior to the relevant JSC meeting.

8.6 The venue for meetings of the JSC will alternate between the premises of the Parties, unless held by teleconference or videoconference. Each Party will be responsible for its own expenses for attendance of JSC meetings including travel and subsistence expenses.

8.7 The JSC shall have the power to invite guests to attend and address JSC meetings. Guests will not be representatives of the JSC and will not have voting rights. The Project Leaders will agree in advance on which Party will bear the costs of engaging a particular guest.

8.8 The current JSC chairperson shall be responsible for promptly preparing the minutes of any JSC meeting, seeking unanimous approval of those minutes from the JSC representatives by signing and dating the approved minutes and promptly distributing a copy of the signed minutes to each Party. It is only such signed and dated minutes that shall constitute a decision of the JSC.

8.9 The JSC shall have the purposes set out below but has no authority to amend, or to waive compliance with, any term or condition of this Agreement. The JSC shall:

8.9.1 guide the overall strategy for the Collaboration Programme including without limitation, discussing the TPP of the Drug Product, development, Manufacturing and Commercialisation activities;

8.9.2 consider and discuss various aspects of the Collaboration Programme, submitted to the JSC by the Project Leaders;

8.9.3 review study protocols and any amendments thereto as part of the Collaboration Programme and any study that may form part of the Regulatory Dossier;

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
8.9.4 make the decision whether to proceed beyond a Holding Point specified in the Development Plan;

8.9.5 make the decision whether to amend the Development Plan and the Regulatory Plan;

8.9.6 review all on-going activities and progress relating to the Collaboration Programme; and

8.9.7 agree a detailed Manufacturing and Supply Plan for the supply of the Drug Product.

8.10 Each Party shall have one vote at the JSC. Conclusions and decisions of the JSC shall be made by agreement whenever possible and recorded in the minutes that are signed and dated by the JSC members. Both Parties will use reasonable endeavours to reach agreement. Any decision made by the JSC through this process shall be binding on the Parties.

8.11 Any differences of opinion between the Parties with regard to the Collaboration Programme shall be discussed in good faith within the JSC. If the JSC is unable to reconcile the opinions within thirty (30) days or to make a decision within the scope of its responsibility, then the Parties shall submit the difference of opinion to each Party’s senior executive officer, which, in the case Entasis, shall be the chief executive officer and, in the case of DNDi, shall be the GARDP Executive Director, to enable a compromise between different views with respect to such issue. If such senior executives of the Parties cannot successfully reconcile the difference of opinion within a fifteen (15) day period after the moment of formal submission to them, then the Party that has responsibility for the performance of the activity in question in its Territory shall have the final decision making authority on such matter, provided, that:

8.11.1 Following the grant of the first Marketing Authorisation, DNDi may conduct Clinical Trials: (a) in DNDi’s Territory without any requirement of consent of Entasis provided that the design of any Clinical Trial with an intent to change the label shall require Entasis’s prior written consent, not to be withheld, conditioned, or delayed unless there are reasonable objections on scientific grounds to the conduct of such Clinical Trial, and (b) in Entasis’s Territory, solely with Entasis’s prior written consent, not to be unreasonably withheld, conditioned, or delayed. Notwithstanding the foregoing, following a Change of Control of Entasis, DNDi will not require the prior consent of any Third Party acquirer to the performance of any Clinical Trial; and

8.11.2 Neither party shall have final decision-making authority with respect to any decision that would restrict or limit the Manufacture or supply of the API or Drug Product in or for the other Party’s respective Territory.

9. SAFETY REPORTING, RECALLS AND INFORMATION EXCHANGE

9.1 Each Party will be responsible for ensuring that it complies with its regulatory obligations as either sponsor or as Marketing Authorisation holder, and for the management of clinical safety and pharmacovigilance with regard to the Drug Product in its respective Territory.

9.2 Within ninety (90) days from the Effective Date or such other period as the Parties may agree before enrolment of the first trial subject in the QT (TQT) Study, the Parties will conclude a pharmacovigilance agreement to govern the investigation of and action to be taken with regard to Drug Product related adverse experience reports, to enable each Party to comply with its legal obligations (“Pharmacovigilance Agreement”).

9.3 Each Party shall exchange with the other Party all relevant information that relates to the safety and efficacy of the Drug Product as set out in the Pharmacovigilance Agreement. Each Party will reasonably co-operate with the other Party to ensure that regulatory requirements concerning drug safety surveillance are complied with in all countries in which the Drug Product is developed, Manufactured or Commercialised both in the Field and for any Future Indications.

9.4 Entasis will be responsible for setting up a worldwide Drug Product safety database, the details of which will be set out in the Pharmacovigilance Agreement.

10. REPRESENTATIONS AND WARRANTIES

10.1 DNDi represents and warrants the following:

10.1.1 It is duly authorized and validly existing under the laws of Switzerland and has full power and authority to enter into this Agreement and to carry out its provisions;

10.1.2 it is duly authorized to execute and deliver this Agreement and perform its obligations hereunder;

10.1.3 the person(s) executing this Agreement on DNDi’s behalf has/have been duly authorized to do so by all requisite corporate action;

10.1.4 this Agreement is a legal and valid obligation binding upon DNDi and enforceable in accordance with its terms. The execution, delivery and performance of this Agreement by DNDi will not: (i) be prevented or impaired by any agreement, instrument or understanding, oral or written to which DNDi is a party or by which it is bound; or (ii) violate any legal requirement to which it is subject;

10.1.5 it shall perform its obligations under this Agreement in accordance with applicable laws and regulations;
10.1.6 as of the Effective Date: (a) it is the sole and exclusive owner or licensee of the entire right title and interest in the DNDi Background Technology; (b) it has not previously entered into any agreement, whether written or oral, with respect to, or otherwise assigned, licensed, transferred, conveyed or otherwise created an encumbrance on its right title and interest in the DNDi Background Technology that would prevent DNDi from granting Entasis rights hereunder, (c) to DNDi’s knowledge, the conception, development and reduction to practice of Patent Rights and Know How relating to the DNDi Background Technology existing as of the Effective Date have not constituted or involved the misappropriation of trade secrets or other rights of property of any person; and (d) DNDi has the right, power and authority to grant all of the rights granted to Entasis hereunder;

10.1.7 DNDi has not received any notice or threat from any Third Party asserting or alleging, nor does DNDi have any knowledge of any basis for any assertion or allegation, that use of the DNDi Background Technology would infringe the intellectual property rights of a Third Party;

10.1.8 during the Term of this Agreement, it will not grant any right to any Third Party any right relating to any portion of the Collaboration Programme any right that would conflict with, limit or adversely affect the rights granted to Entasis hereunder;

10.2 Entasis represents and warrants the following:

10.2.1 It is duly authorized and validly existing under the laws of England and Wales and has full power and authority to enter into this Agreement and to carry out its provisions;

10.2.2 it is duly authorized to execute and deliver this Agreement and perform its obligations hereunder;

10.2.3 the person(s) executing this Agreement on Entasis’s behalf has/have been duly authorized to do so by all requisite corporate action;

10.2.4 this Agreement is a legal and valid obligation binding upon Entasis and enforceable in accordance with its terms. The execution, delivery and performance of this Agreement by Entasis will not: (a) be prevented or impaired by any agreement, instrument or understanding, oral or written to which Entasis or its Affiliates is a party or by which it or they are bound; or (b) violate any legal requirement to which it is or they are subject;

10.2.5 it shall perform its obligations under this Agreement in accordance with applicable laws and regulations;

10.2.6 as of the Effective Date, (a) it is the sole and exclusive owner or licensee of the entire right title and interest in the Entasis Background Technology, (b) it has not previously entered into any agreement, whether written or oral, with respect to, or otherwise assigned, licensed, transferred, conveyed or otherwise created an encumbrance on its right title and interest in the Entasis Background Technology that would prevent Entasis from granting DNDi rights hereunder, (c) to Entasis’s knowledge, the conception, development and reduction to practice of Patent Rights and Know How relating to the Entasis Background Technology existing as of the Effective Date have not constituted or involved the misappropriation of trade secrets or other rights of property of any person; and (d) Entasis has the right, power and authority to grant all of the rights granted to DNDi hereunder;

10.2.7 the Entasis Patent Rights listed in Schedule 3 represent all Patent Rights within Entasis’s Control relating to the Drug Product which as of the Effective Date are necessary for DNDi to perform its obligations hereunder and enjoy the benefit of the licences and rights granted to it hereunder;

10.2.8 Entasis has not received any notice from any Third Party asserting or alleging, nor does Entasis have any knowledge of any basis for any assertion or allegation, that use of the Entasis Background Technology would infringe the intellectual property rights of a Third Party;

10.2.9 the Patent Rights set out in Schedule 3 that have been granted have been properly and correctly maintained in accordance with all applicable laws and all applicable fees have been paid on or before the due date for payment; and

10.2.10 during the Term of this Agreement, it will not grant any right to any Third Party any right relating to any portion of the Collaboration Programme any right that would conflict with, limit or adversely affect the rights granted to DNDi hereunder.

10.3 Each Party represents and warrants to the other Party that:

10.3.1 it will not utilise in connection with the Commercialization of the Drug Product any person or entities that are debarred by any applicable Drug Regulatory Authority;

10.3.2 neither that Party nor its Affiliates nor any director, officer, employee, agent or shareholder of any such person has taken any action that would violate any applicable Anti-Bribery Law nor in the last five (5) years has received any allegation of such violation or has been subjected to any investigation or inquiry by a competent authority relating to any Anti-

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10.3.3 that it has instituted and maintains policies designed to ensure compliance with applicable Anti-Bribery Laws;

10.3.4 the representations and warranties set out in this Clause 10.3 shall remain true and correct at all times;

10.3.5 it will provide written notice to the other Party as soon as practicable and in any event within seven (7) days should such warranty fail to be true or correct.

10.4 A breach of the representations and warranties set out in Clause 10.3 shall be considered a material breach that gives rise to an immediate termination right for the other Party on written notice.

10.5 Each Party shall inform the other Party as soon as reasonably practicable, but in any event within fourteen (14) days, after the occurrence of any of the following events:

10.5.1 cessation of conducting its business or trading;

10.5.2 a Change of Control of it or any of its Affiliates;

10.5.3 sale of all or any material portion of its assets or business to which this Agreement relates;

10.5.4 entry of any declaratory, injunctive or other remedy or court order that would materially impair its ability to conduct its business or perform its obligations under this Agreement;

10.5.5 any attachment or seizure (including prejudgment attachment or seizure) of material assets;

10.5.6 any entry into any restructuring agreement or workout agreement, or similar agreement, relating to any material indebtedness; and

10.5.7 loss of any permits, licences or governmental authorisations that are necessary for it to engage in its current business.

10.6 EXCEPT AS EXPRESSLY SET OUT IN THIS AGREEMENT, EACH PARTY EXPRESSLY DISCLAIMS AND EXCLUDES ANY AND ALL REPRESENTATIONS AND WARRANTIES, EXPRESS OR IMPLIED, STATUTORY OR OTHERWISE, INCLUDING WITHOUT LIMITATION THE WARRANTIES OF MERCHANTABILITY AND FITNESS FOR PURPOSE OR ANY WARRANTY THAT THE PHASE III MC TRIAL OR THE PERFORMANCE OF THE COLLABORATION PROGRAMME WILL PRODUCE ANY PARTICULAR RESULT.

11. INDEMNIFICATION AND LIABILITY

Entasis Indemnities

11.1 Entasis shall defend, indemnify and hold harmless DNDi, its Affiliates and their respective directors, officers, employees and agents (the “DNDi Indemnified Parties”) from and against all Losses arising from or occurring as a result of a Third Party’s claim, action, suit, judgment or settlement to the extent such Losses arise out of:

11.1.1 the negligent conduct of the QT (TQT) Study;

11.1.2 the negligent conduct any Clinical Trial conducted by or on behalf of Entasis or its Affiliates in the context of the Collaboration Programme;

11.1.3 any research and development activities performed by Entasis or its Affiliates outside of the Field;

11.1.4 the Manufacture or Commercialization of the Drug Product by or on behalf of Entasis;

11.1.5 any defects in any Drug Product either supplied by Entasis for the purpose of a Clinical Trial or supplied to DNDi or its Sublicensee by Entasis or its Sublicensee pursuant to any agreed Manufacturing and Supply Plan; and

11.1.6 the negligence, intentional or wrongful acts or omissions or violations of law or regulation by Entasis, its Affiliates or its or their respective directors, officers or employees; and

11.1.7 the breach by Entasis, its Affiliates or its or their respective directors, officers or employees of or the material inaccuracy of, any representation or warranty made by it in Clause 10 of this Agreement.

The foregoing indemnity obligations shall not apply to the extent that any Losses arise from or is based on any activity for which DNDi is obligated to indemnify the Entasis Indemnified Parties under Section 11.2.

DNDi Indemnities

11.2 DNDi shall defend, indemnify and hold harmless Entasis, its Affiliates and its and their respective directors, officers, employees and agents (the “Entasis Indemnified Parties”) from and against all Losses arising from or occurring as a result of a Third Party’s claim, action, suit, judgment or settlement to the extent such Losses arise out of:
11.2.1 any research and development activities performed by DNDi outside of the Field;
11.2.2 the negligent conduct by a DNDi Indemnified Party of the Phase III MC Trial;
11.2.3 the negligent conduct of any other Clinical Trial conducted by or on behalf of DNDi in the context of the Collaboration Programme;
11.2.4 the Manufacture or Commercialization of the Drug Product by or on behalf of DNDi;
11.2.5 the negligence, intentional or wrongful acts or omissions or violations of law or regulation by DNDi, its Affiliates or its or their respective directors, officers or employees; and
11.2.6 the breach by DNDi, its Affiliates or its or their respective directors, officers or employees of or the material inaccuracy of, any representation or warranty made by it in Clause 10 this Agreement.

The foregoing indemnity obligations shall not apply to the extent that any Losses arise from or is based on any activity for which Entasis is obligated to indemnify the DNDi Indemnified Parties under Section 11.1.

11.3 A person entitled to indemnification under Clause 11.1 or 11.2 (an “Indemnified Party”) shall give prompt written notice (the “Indemnification Claim Notice”) through a Party to this Agreement or its insurers to the person from whom indemnification is sought (including where relevant its insurers) (the “Indemnifying Party”) of the threat or commencement of any action, suit or proceeding relating to a Third Party claim for which indemnification may be sought (a “Third Party Claim”). Each Indemnification Claim Notice shall contain a description of the claim and the amount of any Losses claimed. The Indemnifying Party shall promptly provide to the Indemnifying Party copies of all correspondence, communications and official documents (including court documents) received in respect of any such Losses.

11.4 If required, the Indemnifying Party shall notify the insurers of the Third Party Claim and shall permit them to exercise their rights of subrogation.

11.5 Within thirty (30) days after receipt of an Indemnification Claim Notice, the Indemnifying Party shall notify the Indemnified Party in writing whether it intends to control the defence of the Third Party Claim using its legal representatives in which case shall have sole control and responsibility for dealing with the Third Party Claim, including the right to settle the claim provided that:

11.5.1 the Indemnified Party shall be consulted and may retain its own legal representatives for proceedings at its own cost and expense; and

11.5.2 for Losses which are not solely monetary and for which the Indemnified Party has acknowledged in writing an obligation to indemnify or if the Indemnified Party will be subject to injunctive relief, prior written consent of the Indemnified party will be required to settlement (such consent not to be unreasonably withheld).

11.6 If the Indemnifying Party does not assume control of such defence, the Indemnified Party may control such defence provided that the Indemnified Party shall not admit any liability with respect to, or settle, compromise of discharge any such Third Party Claim without the prior written consent of the Indemnifying Party (not to be unreasonably withheld). The Indemnifying Party shall not be liable for any settlement or other disposition of Losses by an Indemnified Party with respect to any Third Party Claim that is entered into without such consent.

11.7 If the Indemnifying Party chooses to defend or prosecute any Third Party Claim, the Indemnified Party that is a Party to this Agreement shall, and shall cause each Indemnified Party to reasonably cooperate in the defence or prosecution thereof and shall provide all records, information and testimony, witnesses and attend such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested in connection therewith. Such cooperation shall include access during normal business hours by the Indemnifying Party to, and reasonable retention by the Indemnified Party of, records and information that are reasonably relevant to such Third Party Claim, and making the Indemnified Party, its Affiliates and its and their respective directors, officers, employees and agents available on a mutually convenient basis to provide additional information and explanation of any records or information provided, and the Indemnifying Party shall reimburse the Indemnified Party for all of its related reasonable out-of-pocket expenses.

11.8 The Party controlling the defence shall keep the other Party advised of the status of such action, suit, proceeding or claim and the defence thereof and shall consider in good faith reasonable recommendations made by the other Party with respect thereto.

Insurance

11.9 Each Party shall maintain at its own cost sufficient insurance to cover its liabilities set out in this Clause 11. Subject to applicable law, the foregoing requirement may be met by way of self-insurance. Upon request from the other Party, each Party shall communicate to the other any

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12.1 This Agreement shall be effective from the Effective Date and, subject to earlier termination in accordance with its terms, it shall remain in force and effect for the duration of the Term. For the avoidance of doubt, at the expiry of the Term in each country of the DNDi Territory and the Entasis Territory, the licences granted by each Party to the other shall become perpetual.

12.2 Each Party shall have the right to terminate this Agreement, without prejudice to any other rights it may have, on ninety (90) days’ written notice if the other Party is in material breach of any of its representations, warranties or obligations hereunder and such breach is either not capable of being remedied, or if capable of being remedied, is not remedied if within thirty (30) days following receipt of the written notice notifying the breaching Party of such breach. If the breach relates to only one country or a group of countries in the Territory of the non-breaching Party, the terminating Party may apply such termination right in relation to the relevant country or countries or to this Agreement as a whole if such breach relates to three or more countries or is unrelated to any specific countries. If the other Party in good faith disputes such material breach or disputes the failure to rectify material breach and provides written notice of that dispute to the other Party within the foregoing timeframe, the matter will be referred for dispute resolution pursuant to Clause 17.2, and the Party wishing to terminate may not do so until it has been determined under Clause 17.2 that the other Party is in material breach of this Agreement and further fails to cure such breach within thirty (30) days after conclusion of that dispute resolution procedure.

12.3 This Agreement may be terminated by either Party upon written notice to the other Party, with immediate effect, in the that any of the following events occurs in relation to the other Party:

12.3.1 a notice has been issued to convene any meeting for the purpose of passing a resolution or seeking a petition to wind up or liquidate that Party, or to seek bankruptcy or official administration, or such a resolution having been passed or such a petition having been issued (except in relation to a solvent reconstruction or reorganisation of that Party);

12.3.2 an involuntary petition in an insolvency proceeding is filed against a Party and is not dismissed or stayed within ninety (90) days of filing thereof; or

12.3.3 a trustee in bankruptcy, receiver, administrative receiver, receiver and manager, court appointed receiver, interim receiver, custodian, sequestrator or similar officer is appointed in respect of that Party or over any part of that Party’s assets or any third party takes steps to appoint such an officer in respect of that Party; or

12.3.4 a Party takes any step, (including starting negotiations), with a view to readjustment, rescheduling or deferral of any part of that Party’s indebtedness including a moratorium with creditors, or proposes or makes and general assignment, composition or arrangement with or for the benefit of all or some of that Party’s creditors or makes or suspends or threatens to suspend making payments to all or some of that Party’s creditors or the Party submits to any type of voluntary arrangement with creditors.

12.4 This Agreement may be terminated by the Parties upon mutual written agreement.

12.5 Either Party may terminate this Agreement at any time after completion or earlier termination of the Phase III MC Trial with twelve (12) months’ prior notice.

12.6 Entasis may terminate this Agreement if DNDi has not achieved the first dosing of the first patient in the Phase III MC Trial within eighteen (18) months after the Effective Date. The foregoing termination right shall not apply if there is a delay in the first dosing of the first patient in the Phase III MC Trial due to:

12.6.1 any act or omission of Entasis or Entasis’s Affiliates or Entasis’s CSPs;

12.6.2 the outcome of any development activities that are required to be conducted prior to the Phase III MC Trial;

12.6.3 delays caused by Drug Regulatory Authorities; or

12.6.4 any Force Majeure event beyond the reasonable control of DNDi.
Consequences of Termination

12.7 In the event of termination by Entasis pursuant to Clause 12.2 (following a final determination by an arbitrator of material breach) or 12.6:

12.7.1 the licenses granted by Entasis to DNDi under Clauses 7.3, 7.5, 7.9 and 7.10, as applicable, shall automatically terminate in so far as they relate to the terminated countries and revert to Entasis and any sublicenses granted thereunder shall automatically terminate and revert to Entasis;

12.7.2 if the entire Agreement is terminated, DNDi shall return to Entasis, or at its request destroy, all Confidential Information and materials received from Entasis pursuant to this Agreement (including in the possession of a Sublicensee);

12.7.3 DNDi shall transfer, or have transferred, to Entasis copies of all relevant Marketing Authorisations in so far as they relate to the terminated countries and, if the entire Agreement is terminated, other documents held by DNDi in relation to the Drug Product within thirty (30) days of termination and shall do all things and execute all documents necessary to give effect to such transfers. If such transfer does not comply with legal requirements for the given country, DNDi shall use reasonable efforts to ensure that Entasis has the benefit of the Marketing Authorisations and consent to any Drug Regulatory Authority to the cross-referencing in the relevant countries to the data and information on file with such Drug Regulatory Authority as may be necessary to facilitate the granting of a second Marketing Authorisation for the Drug Product in the relevant countries. In such circumstances DNDi will, in so far as legally permissible cancel the first Marketing Authorisation for the Drug Product in a country, on the granting of the second Marketing Authorisation. DNDi will further, at its sole cost and expense, complete whatever procedures are necessary or desirable and do all such other acts and things necessary or desirable to enable Entasis (either itself or in conjunction with a Third Party) to develop, Manufacture, and Commercialise the Drug Product in the relevant countries.

12.7.4 the licenses granted by DNDi to Entasis pursuant to Clauses 7.3, 7.7, 7.9, and 7.10 shall survive and become perpetual, worldwide, fully paid up, exclusive, and irrevocable; and

12.7.5 DNDi shall provide the necessary training to any Third Party appointed by Entasis to implement the development of the Drug Product, regulatory activities, Manufacture and Commercialisation or to ensure continuity in the supplies of the Drug Product.

12.8 In the event of termination by DNDi pursuant to Clause 12.2 (following a final determination by an arbitrator of material breach):

12.8.1 the licenses granted by Entasis to DNDi under Clauses 7.3, 7.5, 7.9 and 7.10, as applicable in so far as they relate to the terminated countries, shall become perpetual and irrevocable;

12.8.2 the licenses granted by DNDi to Entasis under Clauses 7.3, 7.7 and 7.9 and 17.10, as applicable in so far as they relate to the terminated countries, shall continue;

12.8.3 to the extent Entasis has not obtained or is not in the process of obtaining Marketing Authorisations in the Field with the FDA, DNDi may file for the first Marketing Authorisation for the Drug Product in the Field with the FDA; provided, that DNDi gives Entasis sixty (60) days’ notice that DNDi plans to file such Marketing Authorisation application. To the extent DNDi obtains Marketing Authorisation from either the FDA, DNDi shall and hereby does grant Entasis an exclusive, royalty-bearing license and right of reference, with the right to grant sublicenses and further rights of reference through multiple tiers, under such Marketing Authorisation with the FDA to Commercialise the Drug Product in the Field in the Entasis Territory. If DNDi obtains a Marketing Authorisation with the FDA and Entasis elects to Commercialize the Drug Product in the United States, then Entasis will pay DNDi a three percent (3%) royalty on net sales (to be defined by the parties at the time of such termination) of Drug Product in the Field in the United States until such time as DNDi recoups one hundred percent (100%) of its out-of-pocket development and regulatory filing costs incurred by DNDi for the Marketing Authorization with the FDA as of the effective date of termination; and

12.8.4 Clause 7.6 shall cease to apply.

12.9 In the event of termination by either Party pursuant to Clause 12.3:

12.9.1 the licenses granted by the insolvent Party to the solvent Party under this Agreement shall become perpetual and irrevocable;

12.9.2 the Parties will negotiate in good faith to address concerns relating to sublicensees in the insolvent Party’s territory; and

12.9.3 if DNDi terminates pursuant to Clause 12.3, to the extent Entasis has not obtained or is not in the process of obtaining Marketing Authorisations in the Field with the FDA, DNDi may

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
12.10 In the event of termination by the Parties pursuant to Clause 12.4, all rights and licenses granted under this Agreement will terminate and each Party shall return to the other, or at the other’s request destroy, all Confidential Information and materials received from the other Party pursuant to this Agreement (including in the possession of a Sublicensee).

12.11 In the event of termination by either Party pursuant to Clause 12.5, the licenses granted to the terminating Party shall terminate and revert to the non-terminating Party, and the licenses granted by the terminating Party to the non-terminating Party under this Agreement shall become perpetual and irrevocable. If Entasis is the terminating Party, at DNDi’s request, Entasis will give DNDi an exclusive first right for a period of ninety (90) days to discuss an opportunity for DNDi to commercialize the Drug Product in one or more countries in the Entasis Territory on mutually acceptable terms. Further, to the extent Entasis has not obtained or is not in the process of obtaining Marketing Authorisations in the Field with the FDA by the end of such ninety (90) day period (or such longer period as the parties may agree), DNDi may file for the first Marketing Authorisation for the Drug Product in the Field with the FDA; provided, that DNDi gives Entasis sixty (60) days’ notice that DNDi plans to file such Marketing Authorisation application. To the extent DNDi obtains Marketing Authorisation from the FDA, unless it is agreed that DNDi will commercialize the Drug Product in the United States, DNDi shall and hereby does grant Entasis an exclusive (except with respect to DNDi as agreed by the Parties after termination), royalty-bearing license and right of reference, with the right to grant sublicenses and further rights of reference through multiple tiers, under such Marketing Authorisation with the FDA to Commercialise the Drug Product in the Field in the Entasis Territory. If DNDi obtains a Marketing Authorisation with the FDA and Entasis elects to Commercialize the Drug Product in the United States, then Entasis will pay DNDi a three percent (3%) royalty on net sales (to be defined by the parties at the time of such termination) of Drug Product in the Field in the United States until such time as DNDi recoups fifty percent (50%) of its out-of-pocket regulatory filing costs incurred by DNDi for the Marketing Authorization with the FDA as of the effective date of termination.

Survival

12.12 Notwithstanding the expiration or termination of this Agreement, and except as provided expressly herein, the provisions of Clauses 1 (to the extent defined terms are contained in the following surviving Clauses), 6.3, 7.1, 7.2, 7.3, each of 7.5, 7.6, 7.7, 7.8, 7.9, 7.10, and 7.14 solely to the extent required under clauses 12.7—12.11, 11.1 (with respect to any matter, fact, or circumstance arising or existing prior to the termination or expiration of this Agreement), 11.2 (with respect to any matter, fact, or circumstance arising or existing prior to the termination or expiration of this Agreement), 11.3, 11.4, 11.5, 11.6 (except as otherwise specified in Clause 12.8 and 12.9) , 11.7, 11.8, 11.9 (for a reasonable period of time following expiration or termination), 11.10, 11.11, 12.1 (as applicable), 12.7 (as applicable), 12.8 (as applicable), 12.9 (as applicable), 12.10 (as applicable), 12.11 (as applicable), this Clause 12.12, 13, 15.1, 16.1, 16.3, 16.7, 16.9, 16.11 (to the extent required under Clauses 12.7—12.11, 16.12, 16.13, and 17 shall remain in full force effect.

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13. CONFIDENTIALITY AND RESTRICTED USE

13.1 Except as specifically set forth elsewhere in this Agreement, each Party shall use only for purposes of this Agreement, and, except as permitted in this Agreement, shall keep confidential and not communicate to any Third Party, all of the Confidential Information received or otherwise learned pursuant to this Agreement including without limitation Confidential Information exchanged prior to the Effective Date relating to the subject matter of this Agreement.

13.2 Each Party shall communicate the Confidential Information of the other Party only to its employees and Third Parties (including, but not limited to actual and potential funding partners, consultants, CSPs and Sublicensees) who need to know such Confidential Information in order to perform this Agreement and who have agreed to abide by confidentiality and restricted use obligations at least as stringent as those set forth herein (the “Permitted Recipients”). Each Party shall be responsible to the other Party for any breach by its Permitted Recipients of such obligations.

13.3 The confidentiality and restricted use obligations set forth herein shall not apply to Confidential Information with respect to which the receiving Party can reasonably prove:

13.3.1 was already lawfully in such Party’s possession at the time of its disclosure hereunder, and not subject to any obligation of confidentiality or restricted use;

13.3.2 is in the public domain at the time of disclosure or becomes in the public domain after disclosure to the receiving Party through no action, fault or omission of the receiving Party;

13.3.3 is lawfully received by the receiving Party from a Third Party, provided that such Third Party is not subject to any obligation of confidentiality or restricted use with respect thereto;

13.3.4 is independently developed by the receiving Party without using any of the Confidential Information received hereunder;

13.3.5 that the receiving Party is required to disclose pursuant to applicable law, regulation or decision or order of any competent court, tribunal, governmental authorities or Drug Regulatory Authority, provided that the receiving Party has promptly disclosed such obligation to the disclosing Party and cooperates with the disclosing Party in efforts to (i) limit the extent of such disclosure to what is required to comply
13.4 The obligations of confidentiality and restricted use in this Clause 13 shall remain in force for the Term of this Agreement and for seven (7) years following disclosure of the relevant Confidential Information.

14. SCIENTIFIC PUBLICATIONS

14.1 Notwithstanding Clause 13, and in accordance with DNDi’s mission statement on providing access to the public of its research, DNDi and Entasis will encourage publications in scientific journals, abstracts or conferences of the scientific data and/or results of the Collaboration Programme pursuant to this Clause 14.

14.2 Each Party shall submit to the other Party prior to publication any draft publication relating to the Collaboration Programme for review at least twenty-eight (28) days prior to the intended date of publication, and permit it to submit comments which the publishing Party shall reasonably take into account, or object to such publication on the grounds that it discloses patentable inventions or discloses confidential technology of a Party. Should Patent Rights be sought by a Party upon any data in the draft publication, publication can be delayed by a maximum period of ninety (90) days to allow for drafting of the Patent Rights application. Each Party will, on the reasonable request from the other Party, remove from any proposed manuscript or presentation any Confidential Information of the other Party provided that neither Party will be prevented from publishing Confidential Information of the other Party (and in particular clinical data) to the extent that publication of such Confidential Information is required for any Regulatory Dossier or in order to obtain a Marketing Authorisation.

14.3 Both Parties will ensure that all written communications, including those that originate from one of their respective partners, indicate that the Drug Product was jointly developed through collaboration between DNDi and Entasis.

15. PUBLICITY

15.1 Except as required by applicable law or the rules of any stock exchange, neither Party shall make any public disclosure concerning this Agreement or the subject matter hereof without the prior written consent of the other Party, which shall not be withheld unreasonably.

15.2 Notwithstanding Clause 15.1, either Party may disclose the information set forth on Schedule 7 (the “Disclosable Information”) without the prior written consent of the other Party, provided that the disclosing Party gives the other Party a copy of or reference (e.g., link to internet site) to such disclosure at the time of disclosure. For the avoidance of doubt, any press release shall require the prior written consent of the non-disclosing Party, even if such press release is limited to the Disclosable Information.

16. MISCELLANEOUS

16.1 Notifications and Communications. All notifications and other communications contemplated by this Agreement shall be sent in writing to the Parties at the following addresses:

For DNDi:
15 Chemin Louis-Dunant
CH-1202 Geneva, Switzerland
Attention: Jean-Pierre Paccaud
With copy to: the GARDP R&D Director

For Entasis:
35 Gatehouse Drive
Waltham, MA 02451
United States of America
Attn: Michael Gutch

or to such other address as the recipient may notify to the other Party in accordance with this Clause 16.1. Unless otherwise set forth herein, all such notifications and communications must be sent by registered letter with return receipt, and shall be deemed delivered on the date on the return receipt (if delivered by registered mail with return receipt requested).

16.2 Entire Agreement; Modification. This Agreement, including the recitals and the Schedules, is the entire agreement, and supersedes all prior agreements, written or oral, between the Parties with respect to the subject matter hereof. No modification of this Agreement shall be effective unless set forth in a writing signed by both Parties.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
16.3 **Invalidity.** If any provision of this Agreement is held to be illegal, invalid or unenforceable under any applicable present or future law, the illegality, invalidity or unenforceability of such provision shall not affect the validity of this Agreement as a whole, unless such provision is of such essential importance for this Agreement that it is to be reasonably assumed that the Parties would not have entered into this Agreement without such provision. Where possible, the Parties shall negotiate in good faith a provision to replace such illegal, invalid or unenforceable provision that is as close to the intent of the original provision as legally possible. All other provisions of this Agreement shall remain valid and in force.

16.4 **Assignment.** Neither Party may transfer or assign to a Third Party any of its rights or obligations under this Agreement without the prior written consent of the other Party, which consent shall not be unreasonably withheld. It is understood, however, that either Party may freely transfer or assign or subcontract any of its rights and obligations under this Agreement to any of its Affiliates. Furthermore, it is understood, that subject to Clause 12.7 either Party may freely transfer or assign or subcontract any of its rights and obligations under this Agreement to any direct or indirect successor to all or substantially all of its business by means of merger, divestment, acquisition, contribution of assets or any other restructuring operation. DNDi may further transfer any of its rights and obligations pursuant to this Agreement to any legal entity that may be set up for the purpose of the business of GARDP (a “GARDP Entity”). DNDi and the GARDP Entity shall provide notice to Entasis of such transfer or assignment to which Entasis shall be deemed to agree by executing this Agreement. Entasis shall, on request and at the cost of DNDi and/or the GARDP Entity enter into any additional documentation that may be required to give effect to or implement any such assignment or transfer.

16.5 **Force Majeure.** Neither Party shall be liable for any default or delay in performing its obligations hereunder if such default or delay is caused by an event of Force Majeure. The Party claiming Force Majeure must promptly inform the other Party of such event and, in accordance with the other Party, must take commercially reasonable endeavours to limit the consequences of such Force Majeure event. If a Party is unable to fulfil any relevant obligation under this Agreement due to any such cause, and this situation continues for a period of six (6) consecutive months, then the other Party may, with immediate effect, terminate this Agreement immediately. In such circumstances the terms set out in Clause 12.7 or 12.8 (as appropriate) shall apply to the Party being terminated.

16.6 **Regulatory Advantages.** The Parties acknowledge that both Parties are actively contributing to the Collaboration Programme hereunder. Consequently, in the event that any advantage may be received from any Drug Regulatory Authority resulting from obtaining any Marketing Authorisation hereunder and arising from the classification of the Drug Product on the WHO essential medicines list the Parties shall discuss in good faith to find a way to share the repercussions of such advantage in an equitable manner.

16.7 **Audit.** Each Party agrees to permit any auditor or an independent public accountant designated by any funding entity of the Collaboration Programme and reasonably acceptable to the Parties to have access, during the Term of this Agreement and for a period of six (6) years from expiry or earlier termination, during regular business hours and upon at least (10) days’ written notice, to its records and books to the extent necessary to determine compliance with the requirements of this Agreement and the Collaboration Programme. The Parties will further agree to appropriate audit rights for the purpose of the Manufacturing and Supply Plan.

16.8 **Amendment.** No amendment, modification or supplement of any provision of this Agreement shall be valid or effective unless made in writing and signed by a duly authorized representative of each Party.

16.9 **Waiver.** No provision of this Agreement shall be waived by any act, omission or knowledge of any Party or its agents or employees except in writing expressly waiving such provision and signed by a duly authorised officer or director of the waiving Party.

16.10 **Counterparts.** This Agreement may be executed in any number of counterparts, each of which need not contain signature on behalf of more than one Party but all such counterparts will, taken together, constitute one and the same agreement. A signed agreement received by a Party hereto and received by way of a pdf submitted electronically will be deemed an original, and binding upon the Party signing it.

16.11 **Further Actions.** Each Party agrees to execute, acknowledge and deliver such further instruments, and do all such other acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

16.12 **Independent Contractors.** The relationship between Entasis and DNDi created by this Agreement is one of independent contractors and neither Party shall have the power or authority to bind or obligate the other. There is no employer-employee relationship, principal-agent relationship, or partnership relationship between Entasis and DNDi or any of their representatives.

16.13 **No Strict Construction; Headings.** This Agreement has been prepared jointly and shall not be construed against either Party. Ambiguities, if any, in this Agreement shall not be construed against any Party, regardless of which Party may be deemed to have authored the ambiguous provision. The headings of each Clause in this Agreement have been inserted for reference only and are not intended to limit or expand the meaning or language in the particular Clause.

17. **GOVERNING LAW AND JURISDICTION**

17.1 This Agreement and any dispute or claim (including non-contractual disputes or claims) arising out of or in connection with this Agreement as a whole, unless such provision is of such essential importance for this Agreement that it is to be reasonably assumed that the Parties would not have entered into this Agreement without such provision. Where possible, the Parties shall negotiate in good faith a provision to replace such illegal, invalid or unenforceable provision that is as close to the intent of the original provision as legally possible. All other provisions of this Agreement shall remain valid and in force.

Subject to Clause 8.11, the Parties shall use reasonable endeavours to resolve amicably any dispute between the Parties arising out of or in connection with this Agreement by referral to the Executive Director of GARDP for DNDi and the Chief Executive Officer for Entasis who shall use reasonable efforts to meet in person within thirty (30) days from written notice of dispute received by one Party from the other. Should such matter remain unresolved at the end of that period, such dispute shall be finally settled under the Rules of Arbitration of the International Chamber of
Commerce by one or more arbitrators appointed in accordance with such rules. The place of arbitration shall be Geneva, Switzerland and the language of the proceedings shall be English.

17.3 Notwithstanding the dispute resolution procedures set forth in Clause 17.2, in the event of an actual or threatened breach of this Agreement, the aggrieved Party may seek provisional equitable relief (including restraining orders, specific performance or other injunctive relief), without first submitting to any dispute resolution procedures hereunder.

17.4 Notwithstanding Clauses 17.1 and 17.2, any dispute concerning the ownership or inventorship of any Patent Rights arising hereunder in any given jurisdiction shall be determined by the courts of the jurisdiction in question.

{SIGNATURE PAGE follows}\n
\[\ast\] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their duly authorized representatives.

Entasis Therapeutics Limited

By: /s/ Manos Perros
Name: Manos Perros
Title: Chief Executive Officer

Drugs for Neglected Diseases initiative

By: /s/ Manica Balasegaram
Name: Dr. Manica Balasegaram
Title: DIRECTOR, GARDP

By: /s/ Jean-Pierre Paccaud
Name: Dr. Jean-Pierre Paccaud
Title: BD and CORPORATE STRATEGY DIRECTOR

{SIGNATURE PAGE folloWS}

\[\ast\] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

Schedule 1: Development Plan

\[\ast\]

\[\ast\] = Twelve pages of certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

Schedule 2: Territories

Entasis Territory

The following countries constitute the Entasis Territory:

\[\ast\]

DNDD Territory

All countries in the world (other than each Additional Country as defined below) that are not specified as being in the Entasis Territory.

Additional Countries

Additional Countries shall be [\ast\] (each an “Additional Country”).

Each Additional Country shall be considered as falling within DNDD’s Territory if, at the time of [\ast\], such Additional Country has either (i) provided investment into development of the API or the Drug Product in the Field by way of funds or contributions in kind with a value of at least EUR [\ast\] or (ii) entered into a binding written commitment (to provide such funds or contributions in kind with a value of at least EUR [\ast\]) during the time the Parties are conducting activities under the Development Plan. Each Additional Country shall be considered as falling within Entasis’s Territory should such foregoing funding condition not be met for such Additional Country.
If an Additional Country is included in DNDi’s Territory at the time of [*], then DNDi shall use commercially reasonable endeavours to obtain a Marketing Authorisation in the Field in such Additional Country. If DNDi has not obtained Marketing Authorization in the Field in such Additional Country within [*], then Entasis will be entitled to transfer that such Additional Country to the Entasis Territory.

If an Additional Country is included in Entasis’s Territory at the time of [*], then Entasis may seek a Marketing Authorisation in the Field in such Additional Country. If Entasis has taken no action to seek Marketing Authorization in the Field in such Additional Country within [*], then DNDi will be entitled to request that such Additional Country be transferred to the DNDi Territory.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

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**Schedule 3: Entasis Patent Rights**

[*]

[*] = Seven pages of certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

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**Schedule 4: Regulatory Plan**

[*]

[*] = Three pages of certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

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**Schedule 5: TPP**

[*]

[*] = One page of certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

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**Schedule 6: API**

[*]

[*] = One page of certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

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**Schedule 7: Disclosable Information**

The Agreement covers and relates to:

- treatment of gonorrhoea caused by *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and/or *Mycoplasma genitalium*
- with drug products containing zoliflodacin
- commercialization by Entasis in certain high-income countries; and commercialization by DNDi in all other countries worldwide
- joint drug development including formulation and clinical and non-clinical studies and subsequent registration
- each party’s commitment to ensure access to the Product.
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