Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the Fiscal Year Ended December 31, 2020

OR

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

For the Transition Period from to

Commission File Number: 001-38670

Entasis Therapeutics Holdings Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**82-4592913**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

35 Gatehouse Drive
Waltham, MA 02451
(781) 810-0120
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

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

Title of each class:	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	**ETTX**	**Nasdaq Global Market**

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Act. Yes ☐ No ☒

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

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

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

Large Accelerated Filer	☐	Accelerated Filer	☐
Non-accelerated Filer	☒	Smaller Reporting Company	☒
Emerging growth company	☒		

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act.) Yes ☐ No ☒

As of June 30, 2020, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of shares of the registrant's common stock held by non-affiliates of the registrant was approximately $39.3 million, based on the closing price of the registrant's common stock on The Nasdaq Global Market on June 30, 2020 of $2.96 per share. The calculation excludes shares of the registrant's common stock held by current executive officers, directors and stockholders that the registrant has concluded are affiliates of the registrant. The determination of affiliate status is not a determination for other purposes.

As of March 17, 2021, there were 37,310,254 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant's definitive proxy statement for its 2021 Annual Meeting of Stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2020, are incorporated by reference into Part III of this Annual Report on Form 10-K.

TABLE OF CONTENTS

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or Exchange Act, and the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical fact are "forward-looking statements" for purposes of this Annual Report on Form 10-K for the fiscal year ended December 31, 2020, or Annual Report on Form 10-K. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "continue," "could," "estimate," "expects," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" or the negative or plural of those terms, and similar expressions. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other "forward-looking" information. Forward-looking statements include, but are not limited to, statements about:

- the severity and duration of the impact of the COVID-19 pandemic on our business, development programs and access to capital;
- our plans to develop and commercialize our product candidates;
- the timing of execution of planned clinical trials and the availability of data from our clinical trials;
- our expectation that the efficacy and safety data from our Phase 3 registration trials, if positive, will be sufficient to support submission of a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA;
- our ability to obtain grants or other government funding to develop our product candidates;
- our ability to take advantage of benefits offered by current and pending legislation related to the development of products addressing antimicrobial resistance;
- the timing of and our ability to file, obtain and maintain regulatory filings for our product candidates;
- the clinical utility of our product candidates and their potential advantages compared to other treatments;
- our commercialization, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for the manufacture of our product candidates;
- our ability to establish and maintain collaborations and to recognize the potential benefits of such collaborations;
- our estimates regarding the market opportunities for our product candidates;
- our intellectual property position and the duration of our patent rights;
- our estimates regarding anticipated operating losses, needs for additional funds and capital requirements;
- political, social and economic instability, natural disasters or public health epidemics in countries where we or our collaborators do business;
- the substantial influence and control that Innoviva, Inc., or Innoviva, may exert on actions requiring stockholder vote; and
- our estimated needs for and ability to raise additional financing, and our ability to continue as a going concern.

Factors that may cause actual results to differ materially from current expectations include, among other things, those set forth in Part I, Item 1A, "Risk Factors," herein and for the reasons described elsewhere in this Annual Report on Form 10-K. These statements involve substantial known and unknown risks, uncertainties and other factors that may

cause our actual results, level of activity, performance or achievements to differ materially from those currently anticipated. Forward-looking statements are neither historical facts nor assurances of future performance.

This Annual Report also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Unless otherwise expressly stated, we obtained this industry, business, market and other data 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 that we cannot independently verify, but believe to be reliable.

In this Annual Report on Form 10-K, unless otherwise stated or as the context otherwise requires, references to “Entasis,” “the Company,” “we,” “us,” “our” and similar references refer to Entasis Therapeutics Holdings Inc. and its wholly owned subsidiaries. The trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

PART I

Item 1. BUSINESS

Overview

We are an advanced, clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of targeted antibacterial products that address high unmet medical needs to treat serious infections caused by multidrug-resistant pathogens.

Our lead product candidate, sulbactam-durlobactam, or SUL-DUR, is an intravenous, or IV, combination of sulbactam, a β-lactam antibiotic, and durlobactam, a novel broad-spectrum β-lactamase inhibitor, or BLI, that we are developing for the treatment of pneumonia and bloodstream infections caused by carbapenem-resistant *Acinetobacter baumannii*, or *Acinetobacter*. Based on current carbapenem resistance rates, we estimate there are in excess of 200,000 hospital-treated carbapenem-resistant *Acinetobacter* infections annually across the United States, Europe, the Middle East and China for which significant morbidity and mortality exists due to limited treatment options. We initiated ATTACK (***A****cinetobacter* **T**reatment **T**rial **A**gainst **C**olistin), our single Phase 3 registration trial in 2019, with top-line data readout expected in the second half of 2021. ATTACK is a global, multi-center trial that will evaluate approximately 120 patients with confirmed carbapenem-resistant *Acinetobacter* hospital-acquired pneumonia, ventilator-acquired pneumonia, ventilated pneumonia or bloodstream infections, or a combination of these. We believe that the data from the ATTACK trial, data from our other clinical trials of SUL-DUR and non-clinical data will be sufficient to submit a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA.

Our second late-stage product candidate, zoliflodacin, is a novel orally administered molecule being developed for the treatment of uncomplicated gonorrhea. The bacterial pathogen responsible for gonorrhea is *Neisseria gonorrhoeae*, or *N. gonorrhoeae*, including multidrug-resistant strains. Intramuscular injections of ceftriaxone now represent the only U.S. Centers for Disease Control and Prevention, or CDC, recommended treatment option for the estimated 1.6 million annual cases of gonorrhea in the United States. We believe there is a growing unmet need for a single-dose oral antibiotic that will reliably treat patients with gonorrhea, including infections caused by multidrug-resistant strains of *N. gonorrhoeae*, which are emerging globally. The Phase 3 registration trial, initiated in September 2019, is a multi-center, open-label, noninferiority trial in approximately 1,000 enrolled patients with uncomplicated gonorrhea. Our nonprofit collaborator, the Global Antibiotic Research and Development Partnership, or GARDP, is the sponsor of the registration trial and is responsible for all trial expenses. We believe data from the Phase 3 registration trial, along with data from our other clinical trials of zoliflodacin and non-clinical data will be sufficient for submitting an NDA to the FDA.

We are also developing ETX0282CPDP for the treatment of complicated urinary tract infections, or cUTIs, including those caused by multidrug-resistant *Enterobacteriaceae*. ETX0282CPDP is an oral combination of ETX0282 with cefpodoxime proxetil. We believe there is a significant unmet need for new oral antibiotics to reliably treat the estimated 3 to 4 million patients diagnosed annually with cUTIs. We have reported preliminary Phase 1 trial results, and subsequently demonstrated that an extended release tablet formulation achieved preclinical proof-of-concept of the desired pharmacokinetic profile both *in vitro* and in non-human primates. Having successfully completed the initial Phase 1 studies and preclinical work to deliver a formulation with the desired extended release profile, we are currently prioritizing our resources on completing the ATTACK trial and supporting the ongoing Phase 3 registration trial for zoliflodacin, while we evaluate options for further clinical development of ETX0282CPDP.

Lastly, we are advancing development of a novel class of antibiotics, non β-lactam inhibitors of penicillin-binding proteins, or NBPs. We believe NBPs constitute a potential new class of Gram-negative antibacterial agents that are designed to target a broad spectrum of multidrug resistant bacterial pathogens that overcome the main source of β-lactam resistance which is driven by β-lactamase activity. This novel class of agent is designed to target a broad spectrum of multidrug resistant bacterial pathogens that are part of the CDC/World Health Organization, or WHO, list of high unmet medical need or ESKAPE pathogens. We selected ETX0462 as the initial clinical candidate for this program, based on demonstrated activity against *Pseudomonas* and a number of high-priority biothreat pathogens combined with a strong preclinical safety profile and attractive physiochemical properties. We currently anticipate completing the

required pre-clinical activities by early 2022 to enable the program to advance into a Phase 1 clinical trial. In June 2020, we were awarded a contract from the National Institute of Health, or NIH, to support research towards developing additional NBP molecules with expanded Gram-negative spectrum from this novel class. This research program, designated NBP2, is attempting to target *Klebsiella, Pseudomonas* and *E. coli* from the ESKAPE list of pathogens. The NIH contract consists of an initial award of approximately $3.0 million, with the potential to increase up to $15.5 million. Subject to achieving pre-defined milestones, the contract is expected to sufficiently fund activities to achieve submission of an Investigational New Drug, or IND, application to the FDA.

Our Strategy

Our goal is to be the leader in the discovery, development and commercialization of targeted antibacterial agents for the treatment of serious infections caused by multidrug-resistant pathogens. Our strategy includes the following key components:

- **Advance our lead product candidate SUL-DUR through the ATTACK Phase 3 registration trial, NDA filing and FDA approval to become the cornerstone of our drug portfolio and, once commercial, to provide cash flow for future company growth.** Our lead product candidate, SUL-DUR, is a novel IV antibiotic that is a combination of sulbactam, an IV β-lactam antibiotic, and durlobactam, our novel BLI, that we are developing for the treatment of a variety of serious infections caused by carbapenem-resistant *Acinetobacter*. We have completed three separate Phase 1 clinical trials and a Phase 2 clinical trial in patients with cUTIs. We initiated ATTACK, our single Phase 3 registration trial in April 2019, that will evaluate SUL-DUR in patients with confirmed carbapenem-resistant *Acinetobacter* pneumonia and/or bloodstream infections. We expect top-line data readout in the second half of 2021. To date we have had three pre-planned Data Safety Monitoring Board, or DSMB, reviews of the trial. Although we remain blinded to the data, the DSMB recommended in each review that the trial be continued without protocol modification. Based on our preclinical efficacy evaluation and the preclinical and clinical tolerability profile of SUL-DUR observed to date, we believe SUL-DUR has the potential to improve outcomes of patients with multidrug-resistant *Acinetobacter* infections, reducing their overall mortality and accelerating their recovery and hospital discharge, leading to reduced healthcare costs. To our knowledge as of the date of this report, there is no other product currently in clinical development for the treatment of infections due to carbapenem-resistant *Acinetobacter.*

- **For advanced drug candidates we will seek to establish an effective and efficient commercialization strategy to enable global access of our product candidates to benefit patients in need and maximize the value of our products.** In the United States, this strategy will be anchored by a lean, focused, specialty sales force, and ex-U.S., we will seek experienced biotechnology/pharmaceutical companies and distribution partners to leverage their global capabilities. For drug candidates that do not necessarily complement a specialty sales force distribution model in the United States, we will either seek partners with relevant commercial capabilities or will look to out-license the products.

- **Develop and maintain a pipeline of pathogen targeted antibiotics for infections poorly treated by existing generic or branded antibiotics.** In addition to SUL-DUR, we believe that our pipeline product candidates present differentiated and compelling solutions for infections caused by certain multidrug resistant pathogens. Zoliflodacin is an oral, potential single-dose treatment for uncomplicated gonorrhea caused by *N. gonorrhoeae*, including multidrug-resistant strains. ETX0282CPDP is a potential treatment of cUTIs, including those caused by multidrug-resistant *Enterobacteriaceae*. ETX0462 is being developed to address multidrug-resistant *Pseudomonas* and biothreat pathogens. Although our current pipeline has been internally generated, additional product candidates may come from either internal research and development or through identification of existing drug candidates that can be in-licensed or collaboratively developed.

- **Leverage existing and establish future collaborations to support our current and future product candidates.** We have collaborated with commercial as well as nonprofit organizations, government agencies and other third parties, including Zai Lab (Shanghai) Co., Ltd. or Zai Lab (Nasdaq: ZLAB),

GARDP, the National Institute of Allergy and Infectious Disease, or NIAID, the U.S. Department of Defense, or DOD, and the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program, or CARB-X, and the Repair Fund, to secure financial and technical support of our research and development efforts.

COVID-19 Business Impact

The COVID-19 pandemic has gripped the world for approximately one year and has had a material impact on the healthcare industry broadly and on us in particular. As patients afflicted with COVID-19 disease continue to reduce hospital intensive care unit, or ICU, and bed capacity and strain healthcare resources, some clinical trial sites in high COVID-19 impact areas have delayed new patient enrollment due to redirection of resources or hospital access restrictions as required by local conditions. Despite these challenges, we and our contract research organization, or CRO, partner have adapted to keep the ATTACK Phase 3 registration trial enrolling throughout the pandemic, and we currently anticipate top-line data readout in the second half of 2021.

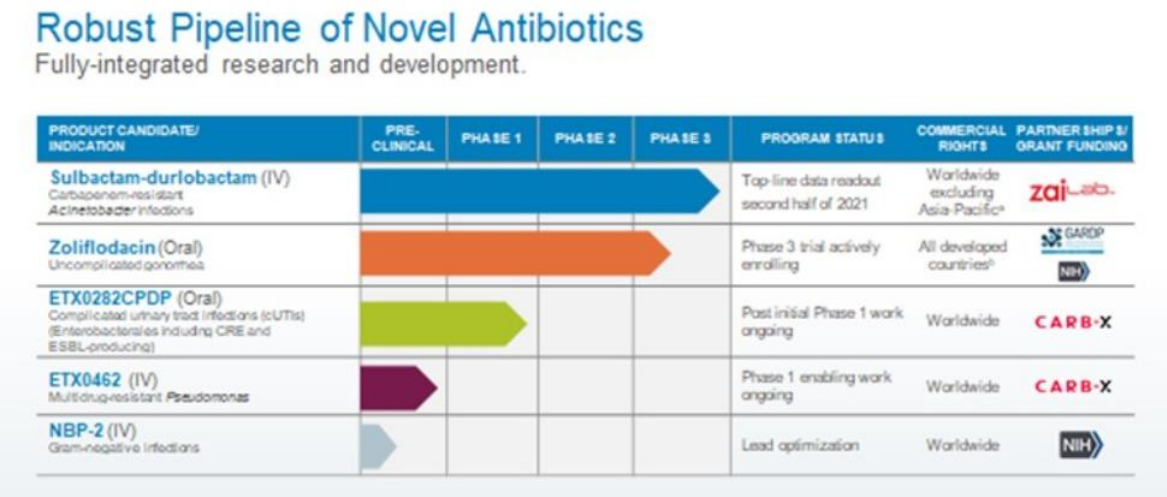
The Company has an Expanded Access Program, or EAP, in place for patients who are not eligible to participate in our ATTACK Phase 3 study and who are suffering from a serious and life-threatening infection caused by drug resistant *Acinetobacter*. Patients co-infected with COVID-19 are eligible if the treating physician feels the risk benefit supports making SUL-DUR available and the patient meets all other conditions needed for consideration of EAP.

The zoliflodacin Phase 3 registration trial also continues to be impacted by the COVID-19 pandemic; however, since July 2020 patient enrollment has resumed at U.S. sites and a clinical trial site in the Netherlands and in January 2021 GARDP announced the activation of our first site in South Africa. We have experienced delays in re-activating some U.S. sites and activating additional clinical trial sites in South Africa and Thailand. Site staff and laboratories are beginning to resume clinical research activities and we anticipate additional site activations in the first half of 2021. Due to the unique challenges posed by the COVID-19 pandemic to this global clinical trial, we remain unable to provide guidance around the timeline for completion of this Phase 3 registration trial. We continue to actively assess the impact of the pandemic on the trial, in consultation with GARDP, and will update when appropriate. To date, there has been no impact to the status of our other product candidates as a result of the COVID-19 pandemic.

Although we are considered an “essential business” for purposes of the state and local stay-at-home orders, the majority of our employees have been working remotely since the issuance of these orders. Our laboratory workers are an exception and operate in reduced and/or staggered shifts in compliance with mandated state guidelines. At this time, we cannot anticipate when we may fully return to an office work environment. As of the date of this report, remote working has had minimal to no impact on our employees, other research and development pipeline programs, our ability to communicate with and manage our key vendors, partners, and drug supply chains, and accurately and timely file our financial statements. Although we are continuing to actively monitor and assess the effects of the COVID-19 pandemic on our business and pipeline programs, the ultimate impact of the COVID-19 pandemic is highly uncertain and subject to change.

Product Portfolio

The following table summarizes the status of our product candidates and preclinical programs:



(1) Zai Lab has licensed exclusive rights to sulbactam-durlobactam in the Asia-Pacific region.

(2) GARDP will fully fund the Phase 3 development program and has commercial rights in World Health Organization, or WHO, defined low-income and specified middle-income countries. We have retained commercial rights in all major markets in North America, Europe and Asia-Pacific.

Antibiotics Background

The introduction of antibiotics for the treatment of bacterial infections is recognized as one of the most transformative events in medicine. Antibiotics either kill bacteria (cytocidal) or inhibit bacterial cell growth (cytostatic), in both cases allowing the body's natural immune system to clear the bacteria. After penicillin, a β-lactam class antibiotic, entered the market in the early 1940s, antibiotics became one of the most commonly prescribed drugs in history. The modern era of antibiotics began in the 1950s with the discovery and commercialization of a number of antibiotic classes and molecules including additional β-lactams, tetracyclines, fluoroquinolones, aminoglycosides and polymyxins.

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 the Enterobacter species, *E. coli*, and *Klebsiella pneumonia*. In the United States, approximately 8.2 million bacterial infections are treated in the hospital annually. Approximately 60% of hospital-treated infections are Gram-negative, and over 140,000 patients treated in the hospital for Gram-negative infections die annually in the United States.

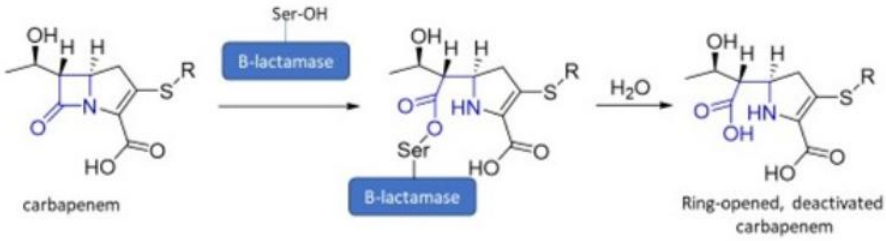
One of the most widely used antibiotic classes are β-lactams due to the combination of their attractive safety and efficacy profile. β-lactams work by inhibiting penicillin binding proteins, or PBPs, proteins that play an important role in bacterial cell wall synthesis and are essential for the growth and reproduction of bacteria. β-lactam antibiotics consist of all antibiotic agents that contain a β-lactam ring in their molecular structures. Among β-lactam antibiotics,

penicillin derivatives and cephalosporins are the most commonly used. Carbapenems, another class of β-lactam antibiotics, are generally more effective against Gram-negative multidrug resistant pathogens; but to preserve their activity, they are often limited for use as a last resort.

Antibiotic Resistance

Antibiotic resistance is a direct consequence of antibiotic use. No sooner was penicillin adopted in clinical use, that the first cases of penicillin-resistant infections were reported. Indeed, resistance to penicillin, as was subsequently found to be the case for other natural product-derived antibiotics, pre-dates its medicinal use. This issue has escalated in the modern era, as millions of metric tons of antibiotics have been produced for human therapeutic use and use in agriculture and animal husbandry. This increased demand and use of antibiotics has contributed significantly to the emergence of resistant strains. For a period, the discovery of new antibiotics kept pace with the emergence of resistance; however, this is no longer the case and as a result, clinicians now commonly resort to using a combination of suboptimal antibiotics in an attempt to treat antibiotic resistant infections. For example, in the United States and European Union from 2004 to 2015, the use of last-resort antibiotics, carbapenems and polymyxins, increased annually by 6% and 8%, respectively. The negative consequences of this approach are twofold, as inappropriate antibiotic therapy leads to poorer outcomes for patients and potential subinhibitory and subtherapeutic antibiotic concentrations can further promote the development of antibiotic resistance.

Antibiotic resistance is now a global health threat and when bacteria develop resistance to at least drugs in three or more antibiotic classes, they are commonly referred to as multidrug-resistant. Bacteria use a number of mechanisms to develop resistance to antibiotics. Resistance to β-lactam antibiotics primarily occurs when bacteria acquire foreign genes that encode β-lactamases, enzymes that inactivate the β-lactam antibiotic by breaking apart the β-lactam ring, which renders the antibiotic inactive. Below, a β-lactamase is shown binding to and cleaving the blue β-lactam ring of a carbapenem antibiotic. β-lactamases are widely prevalent and are classified into four classes, Classes A, B, C and D. Since 1976, researchers have discovered and developed β-lactamase inhibitors (BLIs) that essentially restore the efficacy of the β-lactam antibiotic by neutralizing the β-lactamase enzyme. Despite the discovery and regulatory approval of novel BLIs, current BLIs do not broadly inhibit Class D β-lactamases, which are a particular concern in infections caused by multidrug-resistant *Acinetobacter*.



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, *Acinetobacter*, *Pseudomonas*, CRE and *N. gonorrhoeae*, are all identified as high priority targets by the CDC and WHO, and the Infectious Diseases Society of America, or IDSA.

Rising antibiotic 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. GARDP, NIAID, the Biomedical Advanced Research and Development Authority, or BARDA, the Defense Advanced Research Projects Agency, or DARPA, the DOD, and the Innovative Medicines Initiative, all offer funding or services to support research and development of novel antibiotics.

Changes in the legal/policy landscape in the United States have also highlighted the growing importance of addressing antimicrobial resistance. Proposed legislation includes the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms Act, or DISARM, which calls for payment of qualified infectious disease products, or QIDPs, outside of the hospital diagnosis-related group, or DRG, resulting in potentially higher Medicare reimbursement for those novel antibiotics designated as QIDPs. Qualifying hospitals would be required to participate in a specified antibiotic stewardship program in order to be eligible for higher payment. Most recently, legislation was introduced to the U.S. Senate in September 2020 which aims to reinvigorate innovation for the development of new antibiotics through a subscription contract program managed by the Department of Health and Human Services, or HHS. The Pioneering Antimicrobial Subscriptions to End Upsurging Resistance Act of 2020, or PASTEUR Act, was introduced to provide a mechanism for funding designated 'critical need antimicrobial' drugs following FDA approval. In return, patients covered by federal insurance programs will receive these drugs at no cost. These contracts could range from $750 million to $3 billion in value.

Our Product Candidates

Sulbactam-durlobactam (SUL-DUR)

Overview

Our lead product candidate, SUL-DUR, is a novel IV antibiotic with broad spectrum β-lactamase coverage including Classes A, C and D. The product is a combination of sulbactam, a β-lactam antibiotic, and durlobactam, our novel BLI, that we are developing for the treatment of a variety of serious infections caused by carbapenem-resistant *Acinetobacter*. We have completed three separate Phase 1 clinical trials, including one evaluating the penetration of SUL-DUR into the lung and one in renally impaired patients. In addition, we have completed a Phase 2 clinical trial in patients with cUTIs. We initiated ATTACK, our single Phase 3 registration trial in 2019, that will evaluate SUL-DUR in patients with confirmed carbapenem-resistant *Acinetobacter* pneumonia and/or bloodstream infections. We expect top-line data readout in the second half of 2021. Based on our preclinical efficacy evaluation and the preclinical and clinical tolerability profile of SUL-DUR observed to date, we believe it has the potential to improve outcomes of patients with multidrug-resistant *Acinetobacter* infections, reducing their overall mortality and accelerating their recovery and hospital discharge, leading to reduced healthcare costs.

Acinetobacter

Acinetobacter is a Gram-negative, opportunistic human pathogen that predominantly infects critically ill patients often resulting in severe pneumonia and bloodstream infections, but can also infect other body sites as well. Once thought to be mostly benign, *Acinetobacter* is now considered a global threat in the healthcare setting due in part to its ability to acquire multidrug resistance at rates not previously seen in other bacteria. In addition, *Acinetobacter* has the ability to remain viable for up to 100 days in dry conditions and easily spreads via air or water droplets, which explains why the pathogen can often be found in many locations in the intensive care unit, or ICU, including bedrails, bedside tables, monitors of mechanical ventilators, intravenous pumps, door handles, stethoscopes and many other locations. Of significant concern, one study reported greater than 98% of *Acinetobacter* isolates in an ICU from non-clinical sources such as bedrails and door handles, were determined to be multidrug resistant.

Pneumonia and bloodstream infections caused by drug-resistant *Acinetobacter* can have mortality rates approaching 50%. Antibiotic-resistance rates of *Acinetobacter* to current standard-of-care treatments are some of the highest reported, between 30% and 50% in the United States and greater than 80% in parts of Europe and Asia. *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. There are currently no effective antibiotics indicated for the treatment of multidrug-resistant *Acinetobacter* infections. Durlobactam is the first clinical-stage BLI with sufficient broad-spectrum activity against class A, C, and D β-lactamases to potentially restore the efficacy of β-lactam antibiotics against multidrug-resistant *Acinetobacter*.

Sulbactam, the β-lactam antibiotic used in SUL-DUR has superior microbiological potency against *Acinetobacter* compared to other β-lactam antibiotics based on *in vitro* and *in vivo* analyses. Historically, physicians

used sulbactam to successfully treat *Acinetobacter* infections before development of broad β-lactamase mediated resistance rendered sulbactam on its own largely ineffective. We believe that combining durlobactam with sulbactam can effectively restore the activity of sulbactam against multidrug-resistant strains of *Acinetobacter*.

Market Opportunity

We estimate that there are 180,000 to 220,000 hospital-treated *Acinetobacter* infections annually in the United States and Europe, of which 65,000 to 100,000 are carbapenem-resistant *Acinetobacter* infections, which we regard as our initial target markets for SUL-DUR. We also believe there could be a significant market opportunity in Asia-Pacific, Central and South America, Russia and the Middle East given resistance rates as high as 80% in some countries. If approved, we believe SUL-DUR has the potential to address the issues of resistance facing existing regimens, which is currently limiting the utility of the carbapenems, and tolerability, which is a concern with regimens containing colistin. There are currently no antibiotics indicated for the treatment of carbapenem-resistant *Acinetobacter* infections.

Clinical Development Plan

Ongoing Registration Trial

Phase 3 registration trial: In April 2019, we initiated ATTACK, our global Phase 3 registration trial of SUL-DUR for the treatment of patients with carbapenem-resistant *Acinetobacter* infections. We believe that the efficacy data from this single Phase 3 registration trial, if positive, will be sufficient to support the submission of an NDA to the FDA. The trial is being conducted at approximately 95 sites in 17 countries. ATTACK will evaluate approximately 120 patients with confirmed carbapenem-resistant *Acinetobacter* hospital-acquired pneumonia, ventilator-acquired pneumonia or bloodstream infections, or a combination of these. All patients will be randomized on a 1:1 basis to receive either SUL-DUR plus imipenem, or IMI, or colistin plus IMI over a period of up to 14 days. The primary endpoint will be 28-day all-cause mortality, with a 20% noninferiority margin. As of March 23, 2021, we have randomized 160 patients with *Acinetobacter* infections into Part A, the primary efficacy arm. To complete the Phase 3 registration trial, we need to enroll approximately 120 patients with carbapenem-resistant *Acinetobacter* infections which constitutes the evaluable patients. Not all patients initially randomized into Part A are evaluable for the primary efficacy endpoint. For example, if a patient is enrolled and later determined to have an *Acinetobacter* infection that is not carbapenem resistant or resistant to colistin, the comparator to SUL-DUR, this would disqualify the patient from inclusion in the evaluation for the primary efficacy endpoint. We are currently observing approximately 70% of patients enrolled are evaluable for the primary efficacy endpoint. Based on this evaluable rate, to complete the registration trial will require us to enroll approximately 170 patients with *Acinetobacter* infections to achieve the 120 evaluable carbapenem-resistant patients. Assuming patient enrollment and evaluability rates remain consistent with our experience to-date, we estimate completion of ATTACK enrollment in the coming months with top-line data readout in the second half of 2021.

After enrollment of approximately 40 patients, a per protocol pharmacokinetic, or PK, analysis was conducted to confirm that our projected SUL-DUR exposures in severely ill patients with pneumonia or bloodstream infections are being achieved to maintain our predicted probability of target attainment. Although we remain blinded to treatment assignment, the DSMB has advised us to continue enrollment without modification of the trial protocol and, in addition, has allowed us to open a Part B arm of the trial in 2019, which is an open-label treatment of patients with *Acinetobacter* infections who are not otherwise eligible for the randomized comparison, including those with infections in other body sites such as urinary tract and skin, as well as patients with colistin-resistant *Acinetobacter* infections. These patients will receive SUL-DUR plus IMI. Data from this part of the trial will not be included in the primary endpoint efficacy analysis but will be used in the safety analysis and may provide additional data to support a totality of evidence of SUL-DUR in treating *Acinetobacter* infections. Completion of this per protocol analysis met a program regulatory commitment as discussed with the FDA at the SUL-DUR program end-of-phase 2 milestone meeting. Subsequently, we have had two additional DSMB reviews of the clinical trial, the second review in July 2020 and the third review in February 2021. We remain blinded to the data from these additional reviews, and similar to the initial DSMB review, we have been advised to continue enrollment without modification of the trial protocol.

Pursuant to our license and collaboration agreement with Zai Lab, Zai Lab will enroll up to 20% of the patients from within China and will fund most of the registration trial costs in China for SUL-DUR, except for patient drug supply of the licensed product. Zai Lab will conduct the screening, enrollment and treatment of patients, and will coordinate development, registration and commercialization of SUL-DUR in China. In 2019, Zai Lab received formal approval of the Phase 3 registration trial protocol from the National Medical Products Administration, or NMPA, formerly China Food and Drug Administration. Although Zai Lab continues to enroll patients into the ATTACK Phase 3 registration trial, the total enrollment of *Acinetobacter* patients in China cannot be estimated at this time.

Completed Clinical Trials

We have completed three Phase 1 clinical trials, highlighted below, in addition to a Phase 2 clinical trial in patients with cUTIs. In all of these clinical trials, SUL-DUR was observed to be generally well tolerated.

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

Phase 1 lung trial: Our Phase 1 lung trial assessed the concentration of SUL-DUR in lung fluid, an important metric to understand, because ATTACK includes patients with pneumonia and lack of appropriate lung tissue penetration has been found to contribute to reduced efficacy. We believe that the levels of SUL-DUR in the lung fluid achieved in this trial support its continued development as a potential treatment for pneumonia caused by *Acinetobacter*.

Phase 1 renal trial: Our Phase 1 renal trial analyzed serum levels in renally impaired patients and provided data to enable the development of a dose adjustment protocol for the type of patient targeted in our ongoing Phase 3 registration trial.

Phase 2 clinical trial in cUTI patients: We completed a Phase 2 clinical trial in cUTI patients to provide additional safety and PK data as well as efficacy data against carbapenem-resistant pathogens. Eighty patients were randomized to receive either a dose of SUL-DUR or placebo every six hours for seven days. Patients in both arms also received background therapy, which is current standard-of-care, with 500 mg of IMI administered through IV every six hours.

There were no serious adverse events reported and the adverse event profile of SUL-DUR plus IMI was similar to that of the IMI comparator arm. PK data observed in the Phase 2 trial was consistent with the PK data observed in the Phase 1 clinical trial in healthy volunteers.

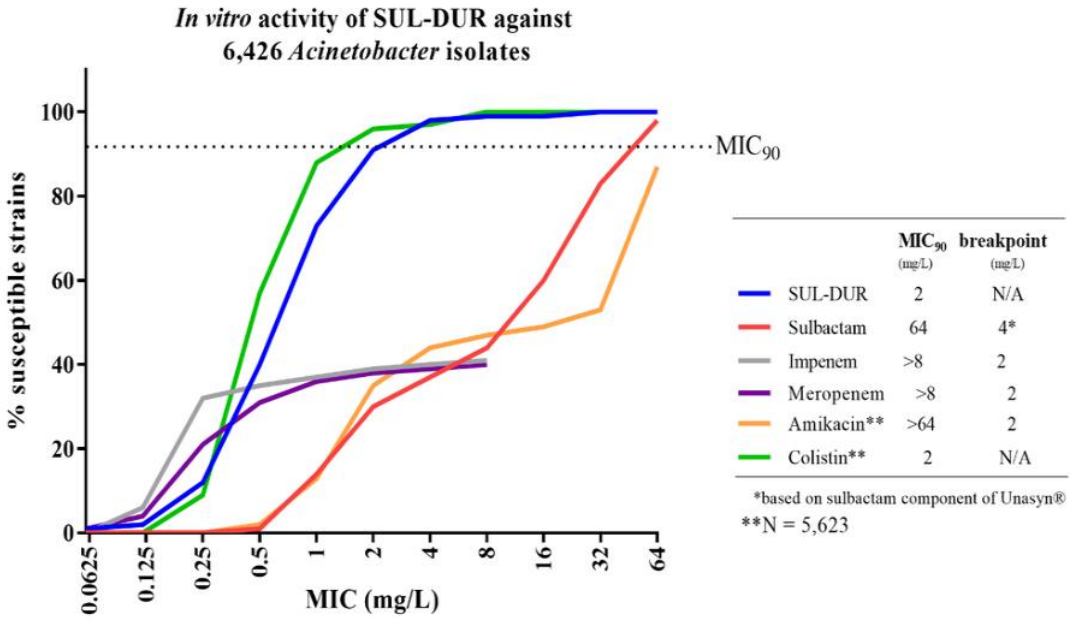
We submitted an investigational new drug application, or IND, for SUL-DUR to the FDA in June 2017, and the FDA notified us in July 2017 that we could proceed with this program. The FDA granted Fast Track and QIDP designation for SUL-DUR in September 2017 for the treatment of hospital-acquired and ventilator-acquired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

Global Acinetobacter Surveillance Data

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

SUL-DUR has also exhibited potent microbiological activity against *Acinetobacter* strains *in vitro.* Over a series of studies summarized in the figure below, we have compared the effectiveness of SUL-DUR, sulbactam alone and comparators in inhibiting 6,426 strains of *Acinetobacter* that were collected from patients around the world between 2011 and 2019. Amikacin and colistin were tested against 5,623 of the 6,426 strains. The plot in the figure below presents the cumulative percentage of these strains inhibited by increasing concentrations of each of the tested compounds. Sulbactam alone, as well as most of the other marketed antibiotics, had a very high MIC_{90} value of 64 mg/L,

meaning that concentrations of 64 mg/L or greater were required to inhibit 90% of the strains. The corresponding breakpoints, which are established by the Clinical & Lab Standards Institute, or CLSI, as 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. This cumulative analysis suggests that recent global strains of *Acinetobacter* are resistant to all the comparator antibiotics other than colistin, consistent with their significantly diminished clinical utility against *Acinetobacter* infections. In contrast, SUL-DUR 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®, a combination of sulbactam and ampicillin), suggesting that our chosen target exposure levels of SUL-DUR may be effective against more than 90% of global, multidrug resistant *Acinetobacter* strains.



Competition

We are initially developing SUL-DUR for the treatment of multidrug-resistant *Acinetobacter* infections. Due to rising resistance rates, standard-of-care treatment for multidrug-resistant *Acinetobacter* infections often includes a combination of several last-line treatment options, including carbapenems, tetracyclines, polymyxins, and other generically available agents. Despite using best available therapy, mortality rates of patients with multidrug-resistant *Acinetobacter* infections is reported as high as 50%. As of the date of this report, we are not aware of any marketed antibiotic that is indicated for the treatment of multidrug-resistant *Acinetobacter* infections; however, we are aware of other potentially competitive products that have shown *in vitro* activity against some strains of *Acinetobacter.* Melinta Therapeutics Inc. currently markets minocycline while La Jolla Pharmaceutical Company, Inc. currently markets eravacycline for complicated intra-abdominal infections. Although recently approved for treating cUTIs, Fetroja®, from Shionogi & Co., Ltd., includes in its label a specific warning of an observed increase in all-cause mortality in patients with carbapenem-resistant Gram-negative bacterial infections that were treated with the drug. As of the date of this filing, ClinicalTrials.gov does not list another program in active clinical development specifically for multidrug-resistant *Acinetobacter* infections.

Manufacturing Approach

We contract with third party contract manufacturing organizations for the manufacture, packaging and labeling of sulbactam and durlobactam for preclinical studies and clinical trials, and we intend to continue to use third party manufacturing organizations in connection with any future commercialization of SUL-DUR. We continue to work with our current manufacturing partners to improve processes to increase our manufacturing capacity, reduce overall cost of manufacturing, and implement other steps toward commercial readiness. Our current manufacturing partners produce drug substance and drug product pursuant to agreements that require compliance with current Good Manufacturing Practices (cGMP). We are currently negotiating commercial supply agreements with third party manufacturing organizations and will look to finalize these agreements as part of commercial readiness.

Commercial Approach

In the United States, we will look to develop our own commercial organization to bring SUL-DUR to market. Our approach is driven by our understanding of where *Acinetobacter* infections are known to exist. Given that *Acinetobacter* infections more commonly occur in immunocompromised patients, these settings are limited in number and well-defined, many of which are less cost-sensitive than average hospital wards.

We are focusing on *Acinetobacter* infections within these settings and to aid in communicating the value proposition of SUL-DUR we have built pharmacoeconomic endpoints into our ATTACK trial. These endpoints include days in the intensive care unit, or ICU, days spent on a ventilator, total days on therapy, and total length of stay vs. standard of care, colistin plus IMI. We believe that with the compelling economic data from our ATTACK trial, a lean, targeted sales force can efficiently reach these key customers and patients.

Current *Acinetobacter* treatment protocols allow for clear positioning of SUL-DUR. Patients with suspected *Acinetobacter* infections are frequently treated with a carbapenem antibiotic as first-line therapy. If susceptibility testing identifies that the causative bacterial pathogen is carbapenem-resistant *Acinetobacter*, the patient is then frequently switched to a colistin-based antibiotic regimen in an attempt to successfully treat the infection. We believe that the ongoing ATTACK Phase 3 registration trial has the potential to demonstrate improved efficacy and safety profiles, and potentially pharmacoeconomic measures that could result in SUL-DUR, if approved, being preferred to a colistin-based regimen for the treatment of multidrug-resistant, including carbapenem-resistant, *Acinetobacter* infections.

Multidrug-resistant *Acinetobacter* infections present a significant unmet medical need in China and across the broader Asia/Pacific territory. Our collaboration and license agreement with Zai Lab, which includes their participation in the ATTACK Phase 3 registration clinical trial, provides a potentially accelerated path for regulatory approval and commercialization in China and Asia-Pacific territories. Zai Lab has been enrolling patients from China into ATTACK. Under our agreement with Zai Lab, we receive upfront, milestone and royalty payments in addition to payment of certain Phase 3 registration clinical trial costs.

We maintain 100% of the rights and associated economics in North America and Europe. Outside of the United States, we intend to work with multi-national pharmaceutical companies to leverage their commercialization capabilities in territories not covered by our agreement with Zai Lab.

Zoliflodacin

Overview

Our second late-stage product candidate is zoliflodacin, a potential single oral dose cure for the treatment of uncomplicated gonorrhea caused by the bacterial pathogen *N. gonorrhoeae*. Gonorrhea is an area of significant medical need and zoliflodacin is the only novel single dose treatment in development that provides a potential monotherapy oral alternative to intramuscular injections of ceftriaxone for the treatment of gonorrhea, including infections caused by drug-resistant strains. Zoliflodacin targets the validated mechanism of action of the fluoroquinolone class of antibiotics but does so in a novel manner to avoid existing fluoroquinolone resistance. We have completed several Phase 1 clinical trials and a Phase 2 clinical trial of zoliflodacin in patients with uncomplicated gonorrhea. In collaboration with GARDP, in 2019 we initiated a single Phase 3 registration trial of zoliflodacin in patients with uncomplicated gonorrhea. GARDP will fund all the Phase 3 development costs and in return will receive commercial rights for zoliflodacin in WHO-defined low-income and select middle-income countries. We have retained commercial rights in all other countries, including the major markets in North America, Europe and Asia-Pacific.

Gonorrhea

Uncomplicated gonorrhea is an *N. gonorrhoeae* infection of the urethra, cervix, pharynx or rectum, and is more common than complicated gonorrhea, which includes spread of the infection to other tissues and potentially the bloodstream. Gonorrhea can be associated with serious complications, including pelvic inflammatory disease, ectopic pregnancy and infertility, as well as an increased risk of human immunodeficiency virus, or HIV. Despite the continued use of effective antibiotics, it remains one of the most common sexually transmitted bacterial infections in the world with an estimated 87 million people worldwide infected each year. The occasional absence of symptoms, more frequent in women, is thought to be one reason for sustained levels of infection. Reports on the lack of a robust immune response to infection by *N. gonorrhoeae* in humans is also thought to facilitate not only initial infection but also reinfection. Efforts to develop a prophylactic vaccine for *N. gonorrhoeae* continue; however, to-date all have failed, again thought to be the result of insufficient or absent protective immunity to *N. gonorrhoeae* infections in humans. Taken together, antibiotics remain the mainstay for treating uncomplicated gonorrhea caused by *N. gonorrhoeae.*

N. gonorrhoeae is the bacterial pathogen responsible for gonorrhea and has a strong propensity for uptake of chromosomal DNA from other genera of *Neisseria* which allows the bacteria to accumulate many mutations in chromosomal genes leading to frequent resistance of antibiotics. For example, penicillin was introduced for *N. gonorrhoeae* infections in 1943, and initial resistance was reported in 1945. Fluoroquinolone antibiotics were first used to treat gonorrhea in 1949 and have been one of the most successful classes of antibiotics against *N. gonorrhoeae*, but even so resistance was identified in 1969. One member of this class, ciprofloxacin, was introduced in 1980 and resistance was identified in 1990. More recently 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, although resistance by *N. gonorrhoeae* has been reported since 2007. As widespread use of these antibiotics drove the emergence of drug-resistant *N. gonorrhoeae* strains, treatment guidelines have subsequently been amended. Ceftriaxone is currently the only CDC-recommended option for the treatment of gonorrhea and, until recently, was administered with azithromycin, a broad-spectrum antibiotic, to provide coverage against other sexually transmitted diseases that tend to occur concurrently with gonorrhea. However, rising resistance of *N. gonorrhoeae* to azithromycin recently prompted the CDC to now recommend ceftriaxone monotherapy. Ceftriaxone is administered by intramuscular injection, which can be painful and may require patient monitoring by a healthcare administrator. Although ceftriaxone remains effective in most of the U.S., in Hawaii as well as in several countries, including China, Japan, France and Spain, *N. gonorrhoeae* strains with resistance to azithromycin and ceftriaxone have been reported, prompting concerns that multidrug-resistant gonorrhea may become a major community health issue.

Market Opportunity

N. gonorrhoeae is an immediate public health threat with 87 million cases worldwide per year (WHO estimate). Reported cases of gonorrhea in the United States have reached an estimated 1.6 million cases per year. In a study based on data from the WHO, it was estimated that in 2017 there were approximately 4.7 million gonorrhea infections in Europe and nearly 35.2 million gonorrhea infections in the Western Pacific region, which includes China and Australia. The CDC estimates that the cases of gonorrhea in the United States have been increasing at least 10% per year since 2009.

The number of countries reporting decreased susceptibility, DS, or resistance, R, to current antibiotics is reflected in the table below.

Antibiotic	Countries with DS or R
Oral ciprofloxacin	70/72 (97%)
Oral azithromycin	47/58 (81%)
Extended spectrum cephalosporins	51/77 (66%)

Historically, to reduce the risk of spreading drug-resistant *N. gonorrhoeae*, the CDC has changed treatment guidelines when resistance rates to recommended first-line treatments reach 5%. Since 2015, there has only been one recommended treatment on CDC guidelines for gonorrhea: 250mg intramuscular injection of ceftriaxone plus 1g of oral azithromycin. The 2020 CDC treatment guideline update follows a 2019 update in the United Kingdom where recommended empirical treatment of gonorrhea is 1g intramuscular ceftriaxone monotherapy.

Clinical Development Plan

Ongoing Registration Trial

Phase 3 registration trial: In 2019 we announced the initiation of a global, multi-center Phase 3 registration trial in collaboration with GARDP who is conducting and funding all Phase 3 development costs. Up to sixteen sites are planned across the U.S., Thailand, South Africa and the Netherlands. Our Phase 3 registration trial is a multi-center, open-label, noninferiority trial in approximately 1,000 enrolled patients with uncomplicated gonorrhea who will be randomized on a 2:1 basis to receive either a single 3.0g oral dose of zoliflodacin or a regimen of 500mg intramuscular ceftriaxone plus 1g oral azithromycin. The primary endpoint will be the proportion of patients with microbiological cure at urethral or cervical sites, approximately six days after treatment. The DSMB in March 2020 recommended to continue the study without modification. Based on our discussions with the FDA, we believe that the efficacy data from this single Phase 3 registration 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.

Completed Clinical Trials

Phase 2 clinical proof-of-concept trial: We have completed a multi-center, randomized, open-label Phase 2 clinical trial comparing a single oral dose of 2.0g or 3.0g of zoliflodacin to 500mg intramuscular ceftriaxone for the treatment of uncomplicated gonorrhea. In this trial, 179 randomized patients received treatment and zoliflodacin was generally well tolerated, with efficacy outcomes comparable to ceftriaxone. 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 rate in both the 3.0g zoliflodacin and ceftriaxone groups in the per-protocol population. The results of this clinical trial were published in *The New England Journal of Medicine* in 2018.

Phase 1 clinical trial: We evaluated zoliflodacin in two Phase 1 clinical trials studying 72 healthy volunteers in total. In one trial, we evaluated PKs 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 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.

Preclinical Data

We have generated biochemical, microbiological and *in vivo* data on zoliflodacin. 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.

Competition

We are initially developing zoliflodacin as a single oral dose treatment for uncomplicated gonorrhea. Gonorrhea is commonly treated with combination therapy intramuscular ceftriaxone injection and oral azithromycin, both generically available agents. Additional generic cephalosporins and fluoroquinolones are also prescribed, but not recommended as primary treatment options given current resistance rates. Gepotidacin, currently under development for a variety of infections by GlaxoSmithKline plc, is the only potentially competitive product candidate in late-stage clinical development that we are aware of that is being developed for the treatment of uncomplicated urogenital gonorrhea. A Phase 3 clinical trial (EAGLE-1) was initiated by GlaxoSmithKline in October 2019. A prior Phase 2 clinical trial indicated emergence of resistance to gepotidacin in 2 urogenital microbiological failures following administration of a single oral dose. In an attempt to overcome this resistance, gepotidacin will be given in two oral doses in the EAGLE-1 clinical trial; a 4-tablet 3000 milligram (mg) oral dose at the study site followed by another 4-tablet 3000mg oral dose as an outpatient.

Manufacturing Approach

GARDP has partnered with third party contract manufacturing organizations for the manufacture of drug substance and drug product for zoliflodacin. These partners are capable of producing commercial scale quantities of zoliflodacin drug substance and drug product under cGMP conditions. GARDP will develop direct long-term commercial supply agreements for sales in their respective territories. As we execute upon our commercialization strategy for zoliflodacin, we intend to work with the established zoliflodacin manufacturing partners for our commercial supply.

Commercial Approach

Zoliflodacin will be available through primary care physicians, outpatient clinics and emergency rooms, and we will seek to contract with payors and distributors who can make the drug accessible to these numerous community sites. We anticipate very low promotional spend as CDC guidelines are expected to drive awareness and uptake. We have partnered with GARDP who will drive the commercialization of zoliflodacin in certain WHO-defined low-income and specified middle-income countries. Outside of the United States, we plan to work with multi-national pharmaceutical companies and/or distributors to leverage their commercialization capabilities in territories not covered by GARDP.

Zoliflodacin is a potential single dose cure (sachet in water) that can facilitate “expedited partner therapy” at home, which may lower the chance for a repeat infection from a partner. Expedited partner therapy, or EPT, is the clinical practice of treating the sex partners of patients diagnosed with chlamydia or gonorrhea by providing prescriptions or medications to the patient to take to his/her partner without the health care provider first examining the

partner. Within the United States, EPT is permissible in 45 states, potentially allowable in 4 states and is only prohibited in one state.

ETX0282CPDP

Overview

Our third product candidate is ETX0282CPDP for the treatment of cUTIs. ETX0282CPDP is an oral, combination of ETX0282, a novel oral BLI, with cefpodoxime proxetil, or cefpodoxime, an oral β-lactam antibiotic. We believe ETX0282 is a highly differentiated oral β-lactamase inhibitor based on its broad inhibition of both Class A and Class C β-lactamases. We selected cefpodoxime as the β-lactam antibiotic to combine with ETX0282 following *in vitro* studies in which cefpodoxime exhibited superior activity against multidrug-resistant *Enterobacteriaceae* compared to other existing oral β-lactams. Cefpodoxime was once used to treat cUTIs, among other indications, but its clinical utility is currently limited by β-lactamase-mediated resistance. We believe ETX0282 has the potential to restore the efficacy of cefpodoxime against multidrug-resistant *Enterobacteriaceae.* We have reported preliminary Phase 1 trial results, and subsequently demonstrated that an extended release tablet formulation achieved preclinical proof-of-concept of the desired pharmacokinetic profile both *in vitro* and in non-human primates. Having successfully completed the initial Phase 1 studies and preclinical work to deliver a formulation with the desired extended release profile, we are currently prioritizing our resources on completing the ATTACK trial and supporting the ongoing Phase 3 registration trial for zoliflodacin, while we evaluate options for further clinical development of ETX0282CPDP.

Urinary Tract Infections

A urinary tract infection, or UTI, diagnosis can be classified as either uncomplicated or complicated. Uncomplicated UTI is an infection of one or more parts of the urinary tract system such as the kidneys, ureters, bladder or urethra with symptoms confined to the lower urinary tract and is often treated with generic oral antibiotics in the community setting. Uncomplicated UTIs, if left unresolved, can have serious consequences, including life-threatening kidney infections. Complicated UTIs, or cUTIs, including pyelonephritis, occur in a urinary tract that has metabolic, functional, or structural abnormality and include patients with comorbidities or patients with bladder catheters. These factors contribute to decreased resolution of such infections and therefore frequently require hospital-based therapy. ETX0282CPDP is being developed for treatment of cUTIs, including those caused by multi-drug resistant *Enterobacteriaceae*, including carbapenem-resistant strains, or CRE. *Enterobacteriaceae* species cause approximately 85% of all UTIs, of which *E. coli* is the most common pathogen, causing approximately 75% of infections. In addition, *Klebsiella* and *Pseudomonas* are also relatively common UTI pathogens. The emergence of multidrug-resistant bacteria has reduced the efficacy of commonly used oral antibiotics such as levofloxacin and ciprofloxacin, both fluoroquinolones, and trimethoprim/sulfamethoxazole. In the United States, over 30% of UTIs caused by *E. coli* and 10% of UTIs caused by *Klebsiella* are resistant to fluoroquinolones.

Market Opportunity

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. In the United States, it is currently estimated that between 3 and 4 million UTIs are treated in the hospital per year. Hospital admission not only leads to inconvenience for the patient and high treatment cost for the healthcare system, but it also increases the risk of transmitting drug-resistant bacterial strains to other hospitalized patients and potentially exposing UTI patients to other, more serious hospital-acquired infections. There are currently no effective oral treatments available for cUTIs, including those caused by multi-drug resistant *Enterobacteriaceae*. If approved, we believe ETX0282CPDP will provide clinicians a convenient, oral option to treat patients suffering from cUTIs caused by these multidrug-resistant pathogens, which could facilitate early hospital discharge following a short course of IV antibiotics or the avoidance of hospital admission altogether. There is also an opportunity for ETX0282CPDP to be used in the broader community setting.

Clinical Development Plan

Phase 1 clinical trial: We conducted a multi-part Phase 1 clinical trial of ETX0282 in Australia and had a preliminary data readout in June 2019. The Phase 1 clinical trial was a randomized, double-blind and placebo-controlled study of ETX0282 alone, not in conjunction with CPDP. The completed cohorts are; Part A: single-ascending dose escalation, fasted; Part B: food effect: fasted versus high fat meal; Part C: multiple dose with regular meals; Part D: drug-drug interaction with regular meals; and Part G: simulation of a high-fat PK profile (fasted).

Overall, the key findings were that ETX0282 was found to be generally safe and well tolerated, no significant adverse events were reported. ETX0282 as the prodrug rapidly converted to ETX1317, the active form of the drug, at all doses. Plasma concentrations were in therapeutic range and the conversion of ETX0282 to ETX1317 was not impacted by multiple dosing and with minimal accumulation. No drug-drug interactions were observed with cefpodoxime. 11 out of 77 subjects receiving ETX0282 experienced mild to moderate emesis (vomiting). The trial data indicated that emesis may be ameliorated by dosing with a high fat meal (not a normal diet). When ETX0282 was dosed in fasted healthy volunteers in a manner to mimic the PK of the high fat meal plus ETX0282 (Part G), no emesis was observed.

Competition

We are initially developing ETX0282CPDP for the treatment of cUTIs. 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 IV approved branded agents targeting multidrug-resistant cUTIs, including Avycaz®, Vabomere®, Zemdri®, as well as the more recently approved IV products Fetroja® (Shionogi & Co., Ltd) and Recarbrio® (Merck & Co., Inc.). We are aware of additional potentially competitive oral product candidates that may address a limited breadth of multidrug-resistant Gram-negative pathogens including sulopenem from Iterum Therapeutics Limited that has completed Phase 3 clinical trials and has received a Prescription Drug User Fee Act, or PDUFA, goal date for completion of the regulatory review of July 25, 2021. Tebipenem from Spero Therapeutics Inc. has also completed a Phase 3 clinical trial and intends to make an NDA submission to the FDA in the second quarter of 2021. An additional potentially competing program in clinical development is Venatorx Pharmaceuticals' Phase 1 NRX-7145, an orally bioavailable beta-lactamase inhibitor (BLI) in a fixed combination with the third generation orally bioavailable cephalosporin, ceftibuten.

ETX0462

Overview

Leveraging our targeted-design platform, we have developed a potential new class of antibiotics that are non-β-lactam penicillin binding protein inhibitors which we are referring to as NBPs. In late 2019, we selected a new drug candidate from our NBP platform, ETX0462, for the potential treatment of multidrug-resistant Gram-negative infections caused by *Pseudomonas* and a number of high-priority biothreat pathogens. If successful in development, we believe our NBPs would be the first, novel Gram-negative antibiotic class since the carbapenems were introduced in 1985. In collaboration with CARB-X, we are advancing this program through registration safety studies and there is an option for support into Phase 1 human studies upon successful completion of the ongoing studies.

Pseudomonas

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

Market Opportunity

Pseudomonas causes a variety of opportunistic 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. This is due in-part to the larger genome compared to other bacteria, which enables *Pseudomonas* to encode enzymes that metabolize, transport and efflux antibiotics. In addition, biofilm formation has been reported in the lungs of patients infected with *Pseudomonas*, which acts as a barrier preventing antibiotic access to the bacteria. *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, including ETX0462, has the potential to be used as monotherapy against infections caused by multidrug-resistant *Pseudomonas*.

Competition

We are initially developing ETX0462 for the treatment of infections caused by multidrug-resistant *Pseudomonas*. There are a variety of generically available antibiotic classes available for the treatment of antibiotic sensitive *Pseudomonas* infections, including cephalosporins, carbapenems and fluoroquinolones. However, there are fewer options for multidrug resistant *Pseudomonas*. Generic polymyxins like Colistin are often utilized in these infections, as are branded IV antibiotics including Avycaz® (Allergan Inc.), Zerbaxa®, and Recarbrio® (both from Merck & Co., Inc.) and Vabomere® (Melinta, Inc.). Cayston® (Gilead Inc.) is an inhaled antibiotic addressing *Pseudomonas* infections in the lungs of cystic fibrosis patients. Zerbaxa® and Cayston® are unfortunately not active when *Pseudomonas* expresses a carbapenemase enzyme, but can potentially overcome other forms of resistance. The other three branded agents are BL/BLI combinations, and *Pseudomonas* has begun to develop resistance to this class of antibiotics via porin channel mutations or efflux pumps. We are aware of additional potentially competitive product candidates in clinical development that may address certain *Pseudomonas* infections including: Ftortiazinon, a small molecule in Phase 2 from the Gamaleya Research Institute (Russia); AR101, a monoclonal antibody in Phase 2 from Aridis Pharmaceuticals Inc.; AP-PA02, a Phase 1 phage candidate from Armata Pharmaceuticals Inc.

Supply and Manufacturing

We do not own or operate manufacturing facilities to produce any of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on third-party contract manufacturers for our required raw materials, drug substance, and finished drug product for our preclinical research and clinical trials. Although we have contracts with these third parties to meet our current clinical supply needs, we do not have any current contractual relationships with these third parties for the manufacture of commercial supply of our product candidates after they are approved. As our product candidates approach potential approval 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 vendor relationships and processes.

Government and Nonprofit Awards

Through December 31, 2020, we have received aggregate financial commitments of up to $21.2 million from the Trustees of Boston University through the CARB-X program, the U.S. Army Medical Research Acquisition Activity, a division of the U.S. Department of Defense, and NIAID in support of our ETX0282, ETX0462, NBP and discovery research programs. The CARB-X awards could provide up to a total of $18.2 million in funding and the NIH award could provide up to a total $15.5 million in funding based on the successful completion of prespecified milestones. These specified milestones include the completion of important steps for a development-stage project such as preclinical studies or clinical trials, manufacture and formulation work, submission of regulatory applications and regulatory meetings with the FDA or comparable foreign regulator.

License and Collaboration Agreements

A significant part of our development and commercial strategy is to partner with established pharmaceutical companies, as well as nonprofit organizations, government agencies and other third parties to provide financial and technical support in the development and marketing of our products.

Zai Lab

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

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

We received an upfront, non-refundable payment of $5.0 million, milestone payments of $7.0 million, research support funding of $0.6 million and certain other reimbursable registration trial costs of $4.2 million, less applicable taxes of $2.1 million from Zai Lab through December 31, 2020. We are eligible to receive up to an aggregate of $91.0 million in additional research and development support payments and development, regulatory and sales milestone payments related to SUL-DUR, imipenem and other combinations with the licensed products. Zai Lab will pay us a tiered royalty equal to a high-single digit to low-double digit percentage based on annual net sales of licensed products in the territory, subject to specified reductions for the market entry of competing products, loss of patent coverage of licensed products and for payments owed to third parties for additional rights necessary to commercialize licensed products in the territory.

Zai Lab may terminate the agreement upon written notice to us at any time and for any reason. Further, we can terminate the agreement if Zai Lab ceases to commercialize the licensed products or challenges any of the patents we licensed to it.

GARDP

In July 2017, we entered into a collaboration agreement with GARDP for the development and commercialization of a product candidate containing zoliflodacin in certain countries. Under the terms of the collaboration agreement, GARDP will use commercially reasonable endeavors to perform and fully fund the Phase 3 registration trial, including the manufacture and supply of the product candidate containing zoliflodacin, in uncomplicated gonorrhea. Both parties are responsible for obtaining marketing authorizations for any future product candidate in such parts of their respective territories as they elect.

In addition, under the collaboration agreement, we have granted GARDP a worldwide, fully paid, exclusive and royalty-free license, with the right to sublicense, to use our zoliflodacin technology in connection with GARDP's development, manufacture and commercialization of zoliflodacin in low-income and specified middle-income countries, which we refer to collectively as the GARDP territory. We have retained commercial rights in all other countries worldwide, including the major markets in North America, Europe and Asia-Pacific. We also have retained the right to use and grant licenses to our zoliflodacin technology to perform our obligations under the collaboration agreement and for any purpose other than gonorrhea or community-acquired indications. GARDP will own all intellectual property developed in its performance under the collaboration agreement regarding formulation development of zoliflodacin. In the event we undertake and fund additional efforts outside of the current agreed-upon development plan for zoliflodacin in our territory that lead to the creation of new intellectual property, we will have a right to file and maintain this new intellectual property. In addition, we are obligated to maintain the intellectual property in the countries in the GARDP territory where we filed patent rights at the date of the agreement and, under specified conditions, in our territory, and GARDP must reimburse us for costs and expenses for the maintenance of such intellectual property rights in the countries of the GARDP territory. If we believe the results of the Phase 3 registration 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. Either party may terminate the collaboration agreement at any time after completion or earlier termination of the Phase 3 registration trial with 12 months' prior notice. We may terminate the collaboration agreement if GARDP has not achieved certain clinical milestones within a specified time period, unless the nonachievement was due to specified types of delay.

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 SUL-DUR, ETX0282 and zoliflodacin.

Pursuant to the terms of the AstraZeneca Agreement, we 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 SUL-DUR. This milestone payment will be automatically waived should our common stock trade on Nasdaq at or above a specified price at the time we achieve such specified cumulative net sales milestone for SUL-DUR, 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. If our board of directors deems the milestone payment obligation related to zoliflodacin to be significantly burdensome, AstraZeneca is required to explore in good faith, modifications to the timing of such payment. At our election, either milestone payment may be paid in cash, shares of our common stock, or a combination of cash and stock. Additionally, we are obligated to pay AstraZeneca tiered, single-digit royalties on the annual worldwide net sales of SUL-DUR and, and the lesser of tiered, single-digit royalties on the worldwide annual net sales of zoliflodacin and a specified share of the royalties we receive from sublicensees of zoliflodacin. Royalties on sales of zoliflodacin do not include sales by GARDP in low-income and select middle-income countries. 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.

See Note 9 , *License and Collaboration Agreements*, and Note 14 , *Commitments*, in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for more information on these collaborations and license agreements.

Intellectual Property

We will be able to protect our technology from unauthorized use by third parties only to the extent it is covered by valid and enforceable patents or is effectively maintained as trade secrets. Patents and other proprietary rights are an essential element of our business.

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 accomplish this we 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 closest to potential commercialization are summarized below.

Durlobactam

Our intellectual property portfolio for our durlobactam program contains patent applications directed to compositions of matter for durlobactam and other chemical analogs, as well as methods of making, referred to as synthetic methods, and methods of use and modes of treatment using durlobactam in combination with one or more antibiotic compounds. As of December 31, 2020, we owned 4 issued U.S. patents, 105 issued foreign patents as well as 14 pending foreign patent applications, of which two are allowed. The issued foreign patents are in several jurisdictions including Australia, the European Union, Canada, China, Hong Kong, Israel, India, Japan, Macau, Mexico, New Zealand, Philippines, the Russian Federation, Singapore, South Africa, South Korea, Taiwan and the United Kingdom. Issued U.S. and foreign patents and patents issuing from pending U.S. and foreign applications will have expiration dates of April 2033 and November 2035.

Zoliflodacin

Our intellectual property portfolio for zoliflodacin contains patent applications directed to compositions of matter for zoliflodacin and other chemical analogs, as well as synthetic methods and methods of use and modes of treatment. As of December 31, 2020, we owned 7 issued U.S. patents, 72 issued foreign patents as well as 17 pending foreign patent applications, of which one is allowed. The issued foreign patents are in several jurisdictions, including Australia, Brazil, Canada, China, Eurasia, the European Union, Hong Kong, India, Israel, Japan, Mexico, New Zealand, Philippines, Singapore, South Africa, South Korea, Taiwan and the United Kingdom. Issued U.S. and foreign patents and patents issuing from pending U.S. and foreign applications have expiration dates of October 2029, January 2034 and May 2035.

ETX0282

Our intellectual property portfolio for our ETX0282 program contains patent applications directed to compositions of matter for the prodrug ETX0282, the active molecule, ETX1317, and other chemical analogs, as well as synthetic methods, and methods of use and modes of treatment using ETX0282 and ETX1317 in combination with one or more antibiotic compounds. As of December 31, 2020, we owned one issued U.S. patent, one pending U.S. application and 19 pending foreign patent applications, of which one is allowed. Issued U.S. and foreign patents and patents issuing from pending U.S. and foreign applications will have expiration dates of September 2037.

ETX0462

Our intellectual property portfolio for our ETX0462 program contains patent applications directed to compositions of matter for ETX0462 and other chemical analogs, as well as synthetic methods, and methods of use and modes of treatment. As of December 31, 2020, we owned one pending U.S. patent application and 20 pending foreign patent applications. Issued U.S. and foreign patents and patents issuing from pending U.S. and foreign applications will have expiration dates of May 2038.

PCT Patent Applications

In addition to the issued and pending patent applications covering our most advanced product candidates, our portfolio also includes one pending PCT application relating to an early stage discovery project.

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, commonly referred to as the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date of a U.S. patent as partial compensation for the length of time the drug is under regulatory review while the patent is in force. A patent term extension cannot extend the remaining term of a patent beyond a total of fourteen years from the date of product approval, only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. We cannot provide any assurance that any patent term extension with respect to any U.S. patent will be obtained and, if obtained, the duration of such extension.

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

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

Intellectual Property from the Collaboration with GARDP

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

intellectual property in the countries in the GARDP territory where we had patents or had filed patent applications prior to the agreement and, under specified conditions, in our territory, and GARDP must reimburse us for costs and expenses for the maintenance of such intellectual property rights in the countries of the GARDP territory.

Intellectual Property from the Collaboration with Zai Lab

In April 2018, we entered into a license and collaboration agreement with Zai Lab for the development and commercialization of products containing durlobactam or SUL-DUR in China and a number of other Asia-Pacific countries, which we refer to collectively as the territory. We retain the right to use our technology to perform our obligations under the agreement and retain the exclusive right to use our technology in all other countries, including North America and Europe. We solely own all rights, title, and interest in all sole or joint patentable inventions that relate to the composition of matter or the method of use of a compound or licensed product. We have the first right to file, prosecute and maintain all licensed patents throughout the world. Zai Lab shall be responsible for reimbursing us for all costs and expenses related to maintaining the licensed patents in the territory.

Trademarks, Trade Secrets and Know-How

Our trademark portfolio currently consists of registered trademark and service mark rights for ENTASIS THERAPEUTICS in several jurisdictions, including the United States, the European Union, Japan, Argentina, Australia, Brazil, Canada, India, Mexico, Norway, the Russian Federation, South Korea, Switzerland, Taiwan, Turkey and the United Kingdom, and pending applications in other jurisdictions. In addition, we have registered trademark rights for ENTASIS THERAPEUTICS (plus design) in the United States, the European Union, Argentina, Brazil, Japan, Australia, India, Norway, the Russian Federation, South Korea, Switzerland, Taiwan, Mexico and the United Kingdom, and pending applications in other jurisdictions. We have also registered trademark rights for XACDURO and XULDURO in the United States, the European Union, Brazil, China, Honk Kong, India, Macau, New Zealand, the Philippines, Taiwan, the United Arab Emirates, Argentina, Malaysia, Saudi Arabia, the United Kingdom, Belarus, Bosnia-Herzegovina, Cambodia, Indonesia, Israel, Laos, Japan, Moldova, Montenegro, Norway, the Russian Federation, Serbia, Singapore, South Korea, Switzerland, Turkey, Ukraine and Vietnam, and pending applications in other jurisdictions. 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 by using invention assignment agreements with our employees. We also have agreements requiring assignment of inventions with selected commercial partners, collaborators, consultants, and scientific advisors. 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 our products and reimbursement. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulation require the expenditure of substantial time and financial resources.

U.S. Government Regulation

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

Approval Processes

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act, or the FDCA, the Public Health Service Act, or PHSA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulation require the expenditure of substantial time and financial resources. Failure to comply with the FDCA and other applicable U.S. requirements at any time during the product development process, approval process or after approval may subject us to a variety of administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include:

- refusal to approve pending applications;
- withdrawal of an approval;
- imposition of a clinical hold;
- warning letters, untitled letters and similar communications;
- product seizures or recalls; or
- total or partial suspension of production or distribution, or injunctions, fines, restitution, disgorgement of profits or civil or criminal investigations and penalties brought by the FDA and the Department of Justice, or DOJ, or other governmental entities.

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 conducted according to Good Laboratory Practices or other applicable regulations;
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use, conducted in accordance with current good clinical practices, or cGCP, which are ethical and scientific quality standards and FDA requirements for conducting, recording and reporting clinical trials to assure that the rights, safety and well-being of trial participants are protected;
- preparation and submission to the FDA of an NDA;

- 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 to assure that the facilities, methods and controls are adequate to preserve the drug's safety, identity, strength, quality and purity; and

- FDA review and approval of the NDA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some preclinical or nonclinical testing may continue even after the IND is submitted. In addition to including the results of the preclinical studies, the IND will also include one or more protocols detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. A clinical hold may occur at any time during the life of an IND and may affect one or more specific studies or all studies conducted under the IND.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with cGCP. They must be conducted under protocols detailing, among other things, the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol and any amendments must be submitted to the FDA as part of the IND, and progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently in other situations, including the occurrence of serious adverse events. An IRB at each institution participating in the clinical trial must review and approve the protocol and any amendments before a clinical trial commences or continues at that institution, approve the information regarding the clinical trial and the informed consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completed and otherwise comply with IRB regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

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

- Phase 1. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, distribution, metabolism and elimination. In the case of some products for severe or life-threatening diseases, such as multidrug-resistant infections, especially when the product may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients with the target disease or condition.

- Phase 2. Clinical trials are initiated in a limited patient population intended 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. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for regulatory approval and product labeling.

Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time for a variety of reasons, including a finding that the research subjects or patients 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.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points, including prior to submission of an IND, at the end of Phase 2 and before an NDA is submitted. Meetings at other times may also be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the end-of-Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial or trials that they believe will support approval of the new drug.

The Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric studies for certain drugs and biologics. Specifically, PREA requires original NDAs, biologic license applications, or BLAs, and supplements thereto for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration to contain a pediatric assessment unless the sponsor has received a deferral or waiver.

Concurrent with clinical trials, companies usually complete additional animal safety studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and the manufacturer must develop methods for testing the quality, purity and potency of the final drugs. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf-life.

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. The submission of an NDA is subject to the payment of user fees, but a waiver of such fees may be obtained under specified circumstances. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to completeness review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth review. NDAs receive either standard or priority review. A drug that, if approved, would represent a significant improvement in the safety or effectiveness of the treatment, prevention or diagnosis of a serious disease or condition may receive priority review. Requests for priority review generally must be submitted at the time of NDA submission. The FDA has agreed to specified performance goals in the review process of NDAs. Under that agreement, 90% of applications seeking approval of new molecular entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten-month and six-month review periods run from the date that FDA receives the application. The review process may be extended by the FDA for three additional months to consider a major amendment to the application following the original submission.

The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing complies with cGMP requirements to assure and preserve the product's safety, identity, strength, quality and purity. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendation.

Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured and tested. These pre-approval inspections may cover all facilities associated with NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP. In addition, the FDA may require, as a condition of approval,

risk evaluation and mitigation strategies, or REMS (which may include requirements for, restricted distribution and use), enhanced labeling, special packaging or labeling, expedited reporting of certain adverse events, pre-approval of promotional materials, restrictions on direct-to-consumer advertising or commitments to conduct additional research post-approval.

On the basis of the FDA's evaluation of the NDA and accompanying information, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. If the FDA ultimately decides that the NDA does not satisfy the criteria for approval, the FDA will issue a complete response letter to indicate that the agency will not approve the NDA in its present form. The complete response letter usually describes all of the specific deficiencies in the NDA identified by the FDA. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application.

Expedited Review and Approval

The FDA has various programs, including Fast Track and priority review, which are intended to expedite or simplify the process for developing and/or reviewing drugs. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Generally, drugs that may be eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the clinical development and expedite the review of drugs to treat serious diseases with the potential, based on nonclinical or clinical data, to fill an unmet medical need. Priority review is designed to give drugs that offer a significant improvement in safety or effectiveness of treatment for a serious condition an expedited review within eight months from the completed submission (six months from filing) as compared to a standard review time of twelve months from the completed submission (10 months from filing) for a standard new molecular entity NDA. Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug and expedite review of the application for a drug designated for priority review.

The Generating Antibiotic Incentives Now Act, or GAIN Act, is intended to provide incentives for the development of new QIDPs. A new drug that is designated as a QIDP after a request by the sponsor that is made before an NDA is submitted will be eligible, if approved, for an additional five years of exclusivity beyond any period of exclusivity to which it would have previously been eligible. In addition, a QIDP will receive priority review and qualify for a Fast Track designation. QIDPs are defined as antibacterial or antifungal drugs intended to treat serious or life-threatening infections, including those caused by an antibacterial or antifungal resistant pathogen or qualifying pathogens identified by the FDA. SUL-DUR has been designated by the FDA as a QIDP for the treatment of hospital-acquired and ventilator-acquired bacterial pneumonia and bloodstream infections due to *Acinetobacter baumannii*. Zoliflodacin has also been designated as a QIDP by the FDA for the treatment of uncomplicated gonorrhea.

Patent Term Restoration and Data Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our drugs, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. As noted above, the Hatch-Waxman Amendments permit a patent restoration term of up to five years for a single patent for an approved product as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of

patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Data exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company using the drug entitled to data exclusivity as the reference listed drug, or RLD. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of data exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the use or conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent for other uses or conditions of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct its own preclinical and clinical studies in support of its application, or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

In addition, as described above, under the GAIN Act a new drug that is designated as a QIDP is eligible for an additional five years of exclusivity to be added to certain other exclusivity periods that the application may qualify for upon approval, specifically five-year exclusivity, three-year exclusivity, and orphan exclusivity.

Pediatric Exclusivity

The Best Pharmaceuticals for Children Act provides for an additional six months of exclusivity, which is added on to patent and exclusivity periods in effect at the time the pediatric exclusivity award is granted, if a sponsor conducts clinical trials in children in response to a written request from the FDA, or a Written Request. The FDA may request studies on approved indications in separate Written Requests. The issuance of a Written Request does not require the sponsor to undertake the described studies. To date, we have not received any Written Requests.

Post-approval Requirements

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, including safety issues, with a product may result in restrictions on the product or even complete withdrawal of the product from the market. 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 FDA review and approval. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. The FDA and other authorities also strictly regulate the promotional claims that may be made about prescription products. Under the FDCA the sponsor of an approved drug in the United States may not promote that drug for unapproved, or off-label, uses, although a physician may prescribe a drug for an off-label use in accordance with the practice of medicine. If we are found to have promoted off-label uses, we may be subject to significant liability, including sanctions, civil and criminal fines and penalties, and injunctions prohibiting us from engaging in specified promotional conduct.

Moreover, any drug products manufactured or distributed pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

- record-keeping requirements;

- reporting of adverse experiences with the drug;
- providing the FDA with updated safety and efficacy information;
- drug sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes;
- complying with certain electronic records and signature requirements; and
- complying with FDA promotion and advertising requirements.

Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP requirements and other laws.

Failure to comply with the FDCA and other applicable U.S. requirements at any time during the product development process, approval process or after approval may subject us to a variety of administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include:

- refusal to approve pending applications;
- withdrawal of an approval;
- imposition of a clinical hold;
- warning letters, untitled letters and similar communications;
- product seizures or recalls;
- total or partial suspension of production or distribution; or
- injunctions, fines, restitution, disgorgement of profits or civil or criminal investigations and penalties brought by the FDA and DOJ, or other governmental entities.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Foreign Regulation

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

Under EU regulatory systems, a company may submit marketing authorization applications under the centralized, decentralized or mutual recognition procedures, or under the purely national route of approval. The centralized procedure is compulsory for medicinal products produced by biotechnology or those medicinal products

containing new active substances for specific indications such as the treatment of acquired immune deficiency syndrome, or AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases, and designated orphan medicines, and is optional for other medicines that are highly innovative. Under the centralized procedure, a marketing application is submitted to the European Medicines Agency, or EMA, where it will be evaluated by the relevant scientific committee, in most cases the Committee for Medicinal Products for Human Use, and a favorable opinion typically results in the grant by the European Commission of a single marketing authorization that is valid for all EU member states and, by extension (after national implementing measures), in Norway, Iceland and Liechtenstein. In general, an initial marketing authorization is valid for five years, but once renewed is usually valid for an unlimited period. The decentralized procedure allows marketing authorization applications to be submitted simultaneously in two or more EU member states, whereas the mutual recognition procedure must be used if the product has already been authorized in at least one other EU member state. Both the decentralized and mutual recognition procedures provide for approval by one or more "concerned" member states based on an assessment of an application performed by one-member state, known as the "reference" member state.

Under the decentralized approval procedure, an applicant submits an application, or dossier, and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must approve the assessment report and related materials, unless they identify a serious risk to public health. Under the mutual recognition procedure, the concerned member states have the same 90-day period to recognize the marketing authorization in the reference member state. In either case, concerns about serious risks to public health escalate through the relevant EMA scientific committees, and the disputed points may eventually result in a consensus opinion from the Committee for Medicinal Products for Human Use that is referred to the European Commission, whose decision is binding on all member states. The purely national procedure results in a marketing authorization in a single EU member state.

Following the result of a referendum in 2016, the United Kingdom left the EU on January 31, 2020, and as of January 1, 2021 the United Kingdom and EU operate separate regulatory regimes. The UK and EU announced on December 24, 2020 that they had agreed a Trade and Cooperation Agreement, or TCA, to govern their future relationship. The TCA remains provisional until formally ratified by the EU, which is expected to occur in early 2021. The TCA sets out the new arrangements for trade of goods, including medicines and medical devices, which aims to ensure goods continue to flow between the EU and the UK and also has implications for product regulation and mutual recognition.

As a result of the United Kingdom's departure from the EU, if a company wishes to sell its products in the United Kingdom, it will need to seek and maintain appropriate national marketing authorizations. The TCA does not provide for wholesale mutual recognition of the regulatory regimes and so products exported from the UK to the EU must comply with the EU's regulatory requirements. In the pharmaceutical context, this has had a number of implications. From January 31, 2020, the UK no longer participated in EU institutions and their decision-making, including approval decisions under the centralized procedure. Moreover, the movement of finished pharmaceutical products into the EU from the UK is treated as an import from a third country. Since the TCA does not provide for mutual recognition of batch testing and release, products must be quality control tested and released in the EU. However, the UK will unilaterally waive batch testing requirements for UK imports from the EU for products placed on the market before January 2023. It remains to be seen how these developments will impact regulatory requirements for product candidates and products in the United Kingdom.

Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of

medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all the approved products for a particular indication.

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

Health Care Laws Governing Interactions with Healthcare Providers

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

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

Federal false claims laws, including the civil False Claims Act, and civil monetary penalties laws prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a claim paid. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal and civil statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any

materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. As with the federal Anti-Kickback Statute, the ACA amended the intent standard for certain healthcare fraud under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it to have committed a violation.

In addition, we may be subject to data privacy and security regulations promulgated by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, impose certain requirements on covered entities (i.e., certain healthcare providers, health plans and healthcare clearinghouses) relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.

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

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

Healthcare and Other Reform

In the United States, there have been and continue to be a number of significant legislative initiatives to contain healthcare costs. Federal and state governments continue to propose and pass legislation designed to reform delivery of, or payment for, healthcare, which include initiatives to reduce the cost of healthcare. For example, in March 2010, the United States Congress enacted the ACA, which expanded health care coverage through Medicaid expansion and the implementation of the individual mandate for health insurance coverage and which included changes to the coverage and reimbursement of drug products under government healthcare programs. Under the Trump administration, there were ongoing efforts to modify or repeal all or certain provisions of the ACA. For example, tax reform legislation was enacted at the end of 2017 that eliminated the tax penalty established under the ACA for individuals who do not maintain mandated health insurance coverage beginning in 2019. The ACA has also been subject to judicial challenge. In December 2018, a federal district court, in a challenge brought by a number of state attorneys general, found the ACA unconstitutional in its entirety because, once Congress repealed the individual mandate provision, there was no longer a basis to rely on Congressional taxing authority to support enactment of the law. In December 2019, the federal appellate court upheld the district court ruling that the individual mandate was unconstitutional and remanded the case back to the district court to determine whether the remaining provisions of the ACA are invalid as well. The case has been appealed to the U.S. Supreme Court where a ruling remains pending.

There were other reform initiatives under the former Trump Administration, including initiatives focused on drug pricing. For example, the Bipartisan Budget Act of 2018 contained various provisions that affect coverage and reimbursement of drugs, including an increase in the discount that manufacturers of Medicare Part D brand name drugs must provide to Medicare Part D beneficiaries during the coverage gap from 50% to 70% starting in 2019. As another example, in 2018, President Trump and the Secretary of the HHS, released a "blueprint" to lower prescription drug prices and out-of-pocket costs. Certain proposals in the blueprint, and related drug pricing measures proposed since the blueprint, could cause significant operational and reimbursement changes for the pharmaceutical industry. HHS has solicited feedback on some of these measures and, at the same, has implemented others under its existing authority. On November 20, 2020, CMS issued an interim final rule through the CMS Innovation Center whereby Medicare Part B reimbursement for "certain high-cost prescriptions drugs" would be no more than most-favored-nation price (i.e., the lowest price) after adjustments, for a pharmaceutical product that the drug manufacturer sells in a member country of the Organization for Economic Cooperation and Development that has a comparable per-capita gross domestic product. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. While some of these and other measures may require additional authorization to become effective, members of Congress and the new Biden administration have indicated that lowering prescription drug prices is a priority, but it is not yet clear what steps the Biden Administration will take or whether such steps will be successful.

There have also been recent state legislative efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices and address 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 2019, the DISARM Act of 2019 was introduced in Congress as new legislation to provide financial incentives for pharmaceutical companies to develop new antibiotics. This new legislation was guided by input from the Infectious Disease Society of America, or IDSA and will help to ensure that patients can access new antibiotics when they are clinically appropriate, require hospitals to establish antibiotic stewardship programs, and spur improved reporting of antibiotic use and resistance to more rapidly identify challenges and inform best practices.

General legislative cost control measures may also affect reimbursement for our product candidates. The Budget Control Act, as amended, resulted in the imposition of 2% reductions in Medicare, but not Medicaid, payments to providers in 2013 and will remain in effect through 2029 unless additional Congressional action is taken. There was a temporary suspension of the 2% reduction during the pandemic; that temporary suspension is scheduled to expire on March 31, 2021. Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented and/or any significant taxes or fees that may be imposed on us could have an adverse impact on our results of operations.

Most recently, legislation was introduced to the U.S. Senate in September 2020 which aims to reinvigorate innovation for the development of new antibiotics through a subscription contract program managed by HHS. The Pioneering Antimicrobial Subscriptions to End Upsurging Resistance Act of 2020, or PASTEUR Act, was introduced to provide a mechanism for funding designated 'critical need antimicrobial' drugs post FDA approval. In return, patients covered by federal insurance programs will receive these drugs at no cost. These Contracts under the PASTEUR Act could range from $750 million to $3 billion in value. It is unclear when or if the PASTEUR Act or similar incentive programs will become law.

Adoption of new legislation at the federal or state level could affect demand for, or pricing of, our current or future products if approved for sale. We cannot, however, predict the ultimate content, timing or effect of any changes to the ACA or other federal and state reform efforts. There is no assurance that federal or state health care reform will not adversely affect our future business and financial results.

Human Capital

As of December 31, 2020, we employed 47 people, all located at our Corporate Headquarters in Waltham, Massachusetts. We have no hourly employees. 12 of our employees work in our laboratory facilities while the remaining

are office personnel. None of our employees are represented by a labor union or covered by a collective bargaining agreement.

The Vice President of Human Resources is responsible for developing and executing our human capital resources strategy. This includes the attraction, acquisition, development, engagement of talent and the design of employee compensation and benefits programs. The Chief Executive Officer and Vice President of Human Resources regularly update our board of directors and our committees on the operation and status of these human capital trends and activities.

Diversity and Inclusion

We have created an environment that fosters individual development while maintaining consistency in our corporate values and code of conduct. In 2020, we signed MassBio's Open Letter 2.0 – The CEO Pledge for a More Equitable & Inclusive Life Sciences Industry. By signing this Pledge, we are committing ourselves to take actions to foster a more diverse and inclusive environment in the life sciences industry.

Health, Safety and Wellness

We strive to provide pay, benefits and other employee services that are competitive to market in the life sciences industry and create incentives to attract and retain employees. Our compensation package includes market-competitive pay, stock options and restrictive stock units, bonuses, employee spot awards, health care and retirement benefits, paid time off and family leave. We utilize third party consultants to review and update our compensation practices annually. We are also committed to the continued development of its people, providing opportunities for employees to further their career development through internal training and education programs and third party online training programs. We have been certified as a “Great Place to Work” for the past two years and we believe our relationship with our employees to be good.

Corporate and Other Information

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

Available Information

You may read our SEC filings, including our proxy statements, annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, over the internet at the SEC’s website at *www.sec.gov*. We also maintain a website at *www.entasistx.com*, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this Annual Report on Form 10-K.

Item 1A. Risk Factors

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

Risk Factor Summary

Risks Resulting from the Current Global Pandemic

- The COVID-19 pandemic has had, and may continue to have, an adverse effect on our business, development programs and access to capital.

Risks Related to Our Financial Position and Capital Needs

- We have incurred significant losses since our inception and we expect to incur losses over the next several years and may never achieve or maintain profitability.
- We require substantial additional funding to be able to continue as a going concern and, 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.
- Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.
- Provisions in the purchase agreement with Innoviva and related documents may deter or prevent us from raising additional capital to fund our options.

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 registration 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.
- If our current clinical trials for our product candidates, including the ATTACK study, 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 our product candidates.
- If we or our collaborators experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

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.

- 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.
- 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 in a timely manner, or such quantities at an acceptable cost or quality.
- 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.

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.
- 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.

Risks Related to Our Business and Managing Our Growth

- We depend on the continuing efforts of our senior management team and other key personnel. If we lose members of our senior management team or other key personnel or are unable to successfully retain, recruit and train qualified researchers, engineering and other personnel, our ability to develop our products could be harmed, and we may be unable to achieve our goals.
- Significant disruptions to our information technology systems or data security incidents could result in significant financial, legal, regulatory, business and reputational harm to us.

Risks Related to Our Intellectual Property

- If we are unable to obtain and maintain patent production 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.

Risks Related to Ownership of Our Common Stock

- Our largest shareholder, Innoviva, holds more than 50% of our common stock and, as a result, may exert a substantial influence on actions requiring stockholder vote, potentially in a manner that you do not support.
- The market price of our common stock is likely to be volatile and could fluctuate or decline, resulting in a substantial loss of your investment.
- The issuance of additional shares of stock, or actual or perceived sales by large holders, could depress the market price of our common stock.
- If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired, which would adversely affect our business.

We have never paid dividends on our capital stock and we do not intend to pay dividends for the foreseeable future.

Risks Resulting from the Current Global Pandemic

The COVID-19 pandemic has had, and may continue to have, an adverse effect on our business, development programs and access to capital, and additional COVID-19 outbreaks may have a similar or worse impact on us.

The COVID-19 pandemic has had, and will continue to have, an unprecedented impact on the U.S. economy in general and large and small businesses in particular. Stay-at-home orders, limitations on building occupancy and sizes of gatherings as well as social distancing requirements have resulted in the closure or limitations on the use of corporate offices and factories and disrupted business operations as employers and workforces adapt to new working conditions and requirements. Since the onset of the pandemic, the majority of our employees have been working remotely and our laboratory workers have operated in reduced and/or staggered shifts. As healthcare systems focus on patients affected by the COVID-19 pandemic, global clinical trials, including our two Phase 3 registration trials, have seen declines in activity or have been suspended temporarily. For instance, for our ATTACK Phase 3 registration trial, some clinical sites in high COVID-19 impact areas periodically delayed new patient enrollment due to redirection of resources or hospital access restrictions as required by local conditions. For our zoliflodacin Phase 3 registration trial, GARDP, with our full agreement, had temporarily paused patient enrollment and activation of new clinical trial sites in March 2020. In June 2020, GARDP resumed patient enrollment into the Phase 3 registration trial at U.S. sites and a new clinical trial site in the Netherlands. However, we have experienced delays in re-activating some U.S. sites and activating additional clinical trial sites in Thailand and South Africa. While we have not experienced material disruptions in our supply chain to date due to the COVID-19 pandemic, it may in the future impact our ability to procure resources, raw materials or components necessary for our development programs. As a result of the unpredictability surrounding the COVID-19 pandemic, the timelines for completion of our registration trials and earlier-stage development programs may be materially impacted. Because the timing, scope and duration of disruptions due to the COVID-19 pandemic are unpredictable, we cannot provide guidance for when we anticipate reporting top-line data or completing our zoliflodacin Phase 3 registration trial. Significant delays in the initiation and completion of our clinical trials or the development of any of our product candidates are costly and could adversely affect our ability to obtain regulatory approval for and successful commercialization of our product candidates. The nature and extent of the impact remains uncertain as the duration of the COVID-19 pandemic and the time needed for businesses and healthcare systems to recover remains unknown. Although we are continuing to actively monitor and assess the effects of the COVID-19 pandemic on our business and development programs, the ultimate impact of the COVID-19 pandemic is highly uncertain and subject to change.

Our ability to raise additional capital may be adversely impacted by worsening global economic conditions and the continuing disruptions to, and volatility in, financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. The continuation of prolonged adverse economic conditions (including due to a resurgence or subsequent waves of COVID-19 infections and delays in completing the distributions of COVID-19 vaccines) could limit our access to financial resources from the capital markets and other sources.

We are not yet certain about the full extent of the long-term potential impact of COVID-19 on our business, development programs and access to capital. To the extent COVID-19 continues to adversely affect our business, financial condition and results of operations, as well as global economic conditions more generally, it may also heighten many of the other risk factors described in this Annual Report on Form 10-K.

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 an advanced, 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 $50.5 million and $43.9 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $184.5 million. We have funded our operations to date primarily with proceeds from the sale of common stock, warrants and convertible preferred stock. We have also either directly received funding or financial commitments from, or have had our program activities conducted and funded by, the U.S. government through our arrangements with the NIH, NIAID, CARB-X, and the DOD, and have received non-profit awards from GARDP, and upfront and milestone payments of $12.0 million, research support funding of $0.6 million and other reimbursable registration trial costs of $4.2 million, less applicable taxes, from our license and collaboration agreement with Zai Lab.

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

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

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

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

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our common stock and could impair our

ability to raise capital, expand our business, maintain our research and development efforts or continue our operations. A decline in the value of our common stock could also cause you to lose all or part of your investment.

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

We commenced active operations in 2015, and our operations to date have been largely focused on raising capital, identifying and developing our product candidates and preclinical program, broadening our expertise in the development of our product candidates, and undertaking preclinical studies and conducting clinical trials. As an organization, we have not yet demonstrated an ability to successfully complete Phase 3 registration 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 be able to continue as a going concern 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.

Absent any additional financing, our cash and cash equivalents as of December 31, 2020 are expected to fund our operating expenses and capital expenditure requirements through the end of the first quarter of 2022, but are not sufficient to sustain our operations in the long term. 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 until at least 2023, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or altogether cease our research and development programs or future commercialization efforts.

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

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

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to a third party to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Provisions in the Company's securities purchase agreement with Innoviva Inc. and related documents may make it more difficult for us to raise additional capital to fund our operations.

Provisions in the agreements we entered into in April 2020 in connection with the First Private may deter or prevent us from raising additional capital to fund our operations as and when needed. For example, the Investor Rights Agreement we entered into with Innoviva in connection with the First Private Placement provides participation rights for Innoviva to participate pro rata in our future offerings of securities. These and other provisions in the First Private Placement documents could deter or prevent us from raising additional capital. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to develop and commercialize our pipeline and otherwise pursue our business strategy and we may be unable to continue as a going concern.

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

As of December 31, 2020, we had U.S. federal and state net operating loss carryforwards, or NOLs, of $119.8 million and $121.2 million, respectively. We do not anticipate generating revenue from sales of products for the foreseeable future, if ever, and we may never achieve profitability. To the extent that we continue to generate tax losses, unused losses generated in tax years ending on or prior to December 31, 2017 will carry forward to offset future taxable income, if any, until such unused losses expire. Unused tax losses generated after December 31, 2017 under the Tax Cuts

and Jobs Act of 2017, or the Tax Act, will not expire and may be carried forward indefinitely, but will be deductible only to the extent of 80% of current taxable income in any given year. It is uncertain if and to what extent various U.S. states will conform to the Tax Act. Under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes to offset its post-change U.S. federal income or U.S. federal taxes may be limited. We have experienced ownership changes in the past and may experience ownership changes in the future and/or subsequent shifts in our share ownership (some of which shifts are outside our control). As a result, if we earn net taxable income for U.S. federal income tax purposes, our ability to use our pre-change NOLs to offset such taxable income may be subject to limitations. Similar provisions of U.S. state tax law may also apply to limit our use of accumulated state tax attributes, including our state NOLs. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes, which could negatively impact our future cash flows.

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 registration 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 our product candidates for the treatment of serious infections caused by multidrug-resistant Gram-negative bacteria. We expect that a substantial portion of our efforts and expenses over the next few years will be devoted to the development of our current product candidates we develop, in-license or acquire. As a result, our business currently depends heavily on the successful development, regulatory approval and, if approved, commercialization of our product candidates. 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. If we do not successfully develop and commercialize product candidates or collaborate with others to do so, we will not be able to obtain product revenue in future periods, which could significantly harm our financial position and adversely affect the trading price of our common stock.

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

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

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

If clinical trials of any of our product candidates 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 that product candidate.

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

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

- the FDA, the EMA or other comparable regulatory authority may change from the views they have expressed to us as to the design or implementation of our clinical trials;
- the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program;
- 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 registration trial;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- we may not be able to complete our clinical trials in a timely manner, if at all, for example because 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;
- we may fail to comply with regulatory requirements applicable to us to FDA's satisfaction;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators may issue a clinical hold, or regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the FDA, the EMA or other comparable regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with whom we enter into agreements for clinical and commercial supplies;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- our product candidates, once exposed to greater numbers of patients, may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the clinical trials;
- even if our clinical trials are successful, the FDA, the EMA or other comparable regulatory authorities may determine that the overall risk-benefit profiles of our product candidates are insufficient to support marketing authorization; 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 our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials or other testing of those product candidates, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

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

Our product development costs may also increase if we experience delays in testing 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 a product candidate.

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 our product candidates, an element of our strategy is to discover, develop and commercialize a portfolio of product candidates to treat serious infections caused by multidrug-resistant Gram-negative bacteria. We are seeking to do so by utilizing our targeted-design platform, which uses bacterial genomics and state-of-the-art molecular and

dynamic models to design active new compounds that target validated mechanisms of resistance. We focus our clinical development on multidrug-resistant pathogens and patients with high, unmet medical needs to leverage the development and regulatory paths available for first-in-class or best-in-class antibiotics. Research efforts to identify and develop product candidates require substantial technical, financial and human resources, whether 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 our current product candidates.

If we or our collaborators 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 our product candidates 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. The challenges of obtaining consent for patient participation have increased during the COVID-19 pandemic as hospitals have imposed restrictions on visitation by friends or family members who may be able to provide consent on behalf of patients. The COVID-19 pandemic may also make patients less willing to seek medical attention or return for follow-up visits post-treatment. 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;
- the risk that patients enrolled in clinical trials will drop out of the trials before completion; and
- the impact of public health epidemics, such as the COVID-19 pandemic.

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 ATTACK may be a potential challenge. Patients enrolled into the clinical trial may have up to 48-hours of prior antimicrobial therapy while identification of *Acinetobacter* using routine microbiologic culture is occurring, but this time window may be insufficient in some cases for identifying *Acinetobacter*, thereby limiting patient enrollment. To address this issue, we are employing an FDA-cleared rapid diagnostic for the identification of *Acinetobacter.* We cannot, however, guarantee that each hospital will utilize this rapid diagnostic as part of their screening and enrollment process or if we will be able to implement the rapid diagnostic in every hospital that is participating in ATTACK. Additionally, patients with *Acinetobacter* infections are generally very sick and, in some cases, may be unconscious and require mechanical ventilation, providing a further potential enrollment challenge. Furthermore, although mortality in some patients is to be expected and is the endpoint of our ongoing Phase 3 registration trial of SUL-DUR, enrollment of near-terminally ill patients could result in a failure to meet our clinical trial endpoints because the patients are too ill to be expected to respond to effective therapy.

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

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

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts (generally referred to as adverse events), to their doctor. We are required to report adverse events to the FDA and other regulatory authorities. Often, it is not possible to determine whether the product candidate being studied caused these conditions. Regulatory authorities may draw different conclusions or require additional testing to confirm these determinations, if they occur. In addition, it is possible that as we test our product candidates in larger, longer and

more extensive clinical programs, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. Many times, side effects are only detectable after investigational drugs are tested in large-scale, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that any of our current product candidates 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.

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

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

Two of our product candidates are β-lactamase inhibitors developed in combination with approved β-lactam antibiotics. If the FDA, the EMA or comparable regulatory authority revokes their approval, we may be unable to obtain approval for our product candidates.

Two of our product candidates 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. Durlobactam is a novel IV, broad-spectrum β-lactamase inhibitor, or BLI, that we are developing in combination with sulbactam, an IV β-lactam antibiotic, for the treatment of a variety of serious multidrug-resistant infections caused by *Acinetobacter*. ETX0282 is a novel, oral BLI that we are developing in combination with cefpodoxime, an oral β-lactam antibiotic, for the treatment of cUTIs, including those caused by *Enterobacteriaceae*.

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

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

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

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

Each of our product candidates, is aimed at treating antibiotic resistant gram-negative bacteria of a specific genus and/or species, such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa* or certain strains of *Enterobacteriaceae.* Typically, when a patient presents with an infection and the bacteria causing the infection is not known or only suspected, a broad-spectrum antibiotic is administered as a first-line empiric treatment pending tests to identify the bacterial pathogen causing the infection and resistance profile. Our product candidates are being developed for use following the identification of the bacterial pathogen and if the resistance profile of the bacterial pathogen suggests that the first-line broad-spectrum antibiotic is not likely to be effective. Our product candidates are designed to

treat specific antibiotic-resistant bacteria where broad-spectrum antibiotics are typically not effective due to the development of antibiotic resistance. However, in those cases when first-line treatment with a broad-spectrum antibiotic has been effective, there would not be a need for second-line treatment with our product candidates. If the bacteria we target become less resistant to existing broad-spectrum antibiotics, or if new broad-spectrum antibiotics are developed that are equally effective against the specific bacteria we target, then the potential demand for our product candidates could be diminished.

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

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 our 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. Additionally, our product development programs and the commercialization of our product candidates will require substantial additional cash to fund expenses. As a result of these factors, we are, and expect to continue to be, dependent on collaborations relating to the development and commercialization of our existing and future product candidates. We currently have a collaborative relationship with Zai Lab to develop durlobactam and SUL-DUR in the Asia-Pacific region and with GARDP to develop zoliflodacin in a Phase 3 registration 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 and we may face significant competition in seeking appropriate collaborators. If we fail to enter into or maintain collaborations on reasonable terms or at all, our ability to develop our existing or future product candidates could be delayed, the commercial potential of our products could change, and our costs of development and commercialization could increase. If we enter into any future collaboration arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

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

- collaborators often have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected or contractually obligated;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products;

- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

- collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;

- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;

- collaborators may be subject to geo-political actions, natural disasters or other occurrences, including public health epidemics such as the coronavirus currently impacting China and elsewhere;

- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates; and

- collaborators' decisions may limit the availability of the product supplies required for development, clinical and commercial activities.

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

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

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

Although Zai Lab and GARDP are each responsible for conducting specified Phase 3 registration trial activities, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on our collaborators does not relieve us of our regulatory responsibilities. We are required to comply with GCP for any product candidate of ours in clinical development. Regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators and clinical

trial sites. If we fail to comply with applicable GCP, the clinical data generated in our trials may be deemed unreliable and the FDA or foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. In addition, we must conduct our clinical trials with drug product manufactured under current good manufacturing practices, or cGMP, requirements. Failure to comply with any of these regulations may require us to repeat preclinical studies and clinical trials, which would delay the regulatory approval process.

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

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

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

In addition, we plan to develop certain 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 durlobactam, ETX0282 or any of our future product candidates, we may not be able to complete clinical development of our product candidates on our current timeline or at all.

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

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

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- supply chain disruptions due to geo-political actions, natural disasters or public healthy crises, including epidemics such as the coronavirus.

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 the approved drugs 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.

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

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

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

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

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

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

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

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

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

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

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

Risks Related to the Commercialization of Our Product Candidates

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

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

If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire a sales force in the United States that is sufficient in size or has adequate expertise to target the hospital setting that we intend to target. If we are unable to establish a sales force and marketing and distribution capabilities, our operating results may be adversely affected.

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

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

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

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

Even if we obtain approvals from the FDA, the EMA or other comparable regulatory agencies and can initiate commercialization of a product candidate we develop, the product candidate may not achieve market acceptance among physicians, patients, hospitals, including pharmacy directors, and third-party payors and, ultimately, may not be commercially successful. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- the potential and perceived advantages and disadvantages of the product candidates, including cost and clinical benefit relative to alternative treatments;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- acceptance by physicians, patients, operators of hospitals, including in-hospital formularies, and treatment facilities and parties responsible for coverage and reimbursement of the product;
- the availability of coverage and adequate reimbursement by third-party payors and government authorities;
- the ability to manufacture our product in sufficient quantities and yields;
- the strength and effectiveness of marketing and distribution support;
- the prevalence and severity of any side effects;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling or an approved REMS;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular infections;
- the approval of other new products for the same indications;
- the timing of market introduction of the approved product as well as competitive products;
- the emergence of bacterial resistance to the product; and
- the rate at which resistance to other drugs in the target infections grow.

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

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

The development and commercialization of new drug products is highly competitive. We face competition from major multi-national pharmaceutical companies, biotechnology companies, specialty pharmaceutical companies and

generic drug companies with respect to our current and future product candidates. There are several large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of drug-resistant infections. Potential competitors also include academic institutions, government agencies and other public and private research organizations. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective, more effectively marketed and sold or less costly than our product candidates, which could render our product candidates non-competitive and obsolete.

We are initially developing SUL-DUR for the treatment of pneumonia and bloodstream infections caused by multidrug-resistant *Acinetobacter*. Due to rising resistance rates, standard-of-care treatment for multidrug-resistant *Acinetobacter* often includes a combination of several last-line treatment options, including carbapenems, tetracyclines and polymyxins, all generically available agents. As of the date of this report, we are not aware of any marketed antibiotic that is indicated for the treatment of multidrug-resistant *Acinetobacter* infections; however, we are aware of other potentially competitive products that have shown *in vitro* activity against some strains of *Acinetobacter.*

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

We are initially developing ETX0282CPDP for the treatment of cUTIs, including those caused by multidrug-resistant *Enterobacteriaceae*. 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 IV approved branded agents targeting multidrug-resistant cUTIs. We are aware of additional potentially competitive oral product candidates that may address a limited breadth of multidrug-resistant Gram-negative pathogens.

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

A primary trend in the United States 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.

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

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

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

- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods, fires, and public health epidemics, such as the coronavirus outbreak currently impacting China and elsewhere.

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

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, David Altarac, M.D., our chief medical officer, John Mueller, Ph.D., our chief development officer, Ruben Tommasi, Ph.D., our chief scientific officer, and Matt Ronsheim, Ph.D., our chief pharmaceutical sciences and manufacturing officer, as well as the other members of our scientific and clinical teams. Although we have employment agreements with our executive officers, each of them may nevertheless terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or employees.

Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of any of our product candidates, commercialization, manufacturing and sales and marketing personnel, will be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize our product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high-quality personnel, our ability to pursue our growth strategy will be limited.

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

As of December 31, 2020 we had 47 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.

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 adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our technology and product candidates. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and erode or negate any competitive advantage that we may have, which could harm our business and ability to achieve profitability. To protect our proprietary positions, we file patent applications in the United States and abroad related to our novel technologies and product candidates that are important to our business.

The patent application and prosecution process are expensive and time-consuming. We and our current licensees, or any future licensors and licensees may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We or our current licensees, or any future licensors or licensees may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection.

Therefore, these and any of our patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If our current licensees, or any future licensors or licensees, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised, and we might not be able to prevent third parties from making, using and selling competing products. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and/or 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. For example, European patent law currently restricts the patentability of methods of treatment of the human body more than United States law does. In addition, the determination of patent rights with respect to pharmaceutical compounds and technologies commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Furthermore, recent changes in patent laws in the United States, including the America Invents Act of 2011, may affect the scope, strength and enforceability of our patent rights or the nature of proceedings that may be brought by us related to our patent rights.

We may not be aware of all third-party intellectual property rights potentially relating to our current and future our product candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Similarly, should we own any patents or patent applications in the future, we may not be certain that we were the first to file for patent protection for the inventions claimed in such patents or patent applications. As a result, the issuance, scope, validity and commercial value of our patent rights cannot be predicted with any certainty. Moreover, we may be subject to a third-party pre-issuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become

involved in derivation, ex-parte reexamination, or *inter partes* review proceedings in the USPTO or similar proceedings 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. If the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

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, a patent being held unenforceable, and/or in one or more or in patent claims being narrowed or 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.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the U.S., if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest filing date of a non-provisional application to which the patent claims priority. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product candidate, we may be open to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours.

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. Depending upon the timing, duration and conditions of any FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union, as discussed above. As a result, our revenue from applicable products could be reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case, and our competitive position, business, financial condition, results of operations, and prospects could be materially harmed.

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 and other third parties 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 or that one or more claims of a patent are invalid, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the basis that our patents do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

In any infringement litigation, any award of monetary damages we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive because of the proceedings. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing, misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a negative impact on our ability to compete in the marketplace.

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

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

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our technology or product candidates, including interference proceedings before the USPTO. Intellectual property disputes arise in several areas including with respect to patents, use of other proprietary rights and the contractual terms of license arrangements. Third parties may assert claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance.

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

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

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

If we are unable to obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology and product candidates, which could materially harm our business, financial condition, results of operations, and prospects.

We may be subject to claims by third parties asserting that we or our employees, consultants or contractors have wrongfully used or disclosed confidential information of third parties, or we have wrongfully used or disclosed alleged trade secrets of their current or former employers, or claims asserting we 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 in 2015 as a spin-out from AstraZeneca AB, or AstraZeneca. Although all patent applications are fully owned by us and were either filed by AstraZeneca with all rights fully transferred to us, or filed in our sole name, because we acquired certain of our patents from AstraZeneca, we must rely on their prior practices, regarding the assignment of such intellectual property. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A court could prohibit us from using technologies or features that are essential to our products if such technologies or features are found to incorporate or be derived from the trade secrets or

other proprietary information of the former employers. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and could be a distraction to management. In addition, any litigation or threat thereof may adversely affect our ability to hire employees or contract with independent service providers. Moreover, a loss of key personnel or their work product could hamper or prevent our ability to commercialize our products.

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

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

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

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

In addition to seeking patent and trademark protection for our product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties prior to beginning research or disclosing proprietary information. 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. Despite these efforts and the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information due to our reliance on third parties, increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements.

Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

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

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

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In some cases, we may not be able to obtain patent protection for certain licensed technology outside the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we do pursue patent protection or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Competitors may use our technologies in jurisdictions where we have not 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 more narrowly than we anticipate, which could limit sales of the product.

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

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

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

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

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

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 REMS, 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. We must also comply with FDA requirements for adverse event reporting for commercial products.

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 U.K. and 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 U.K.'s or EU's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

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

We are exposed to the risk of employee fraud or other misconduct or failure to comply with applicable regulatory requirements. Misconduct by employees and independent contractors, such as principal investigators, CROs, consultants, commercial partners and vendors, could include failures to comply with regulations of the FDA, the EMA and other comparable regulatory authorities, to provide accurate information to such regulators, to comply with manufacturing standards we have established, to comply with healthcare fraud and abuse laws, to report financial information or data accurately or to disclose unauthorized activities to us. Sales, marketing and other business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of business activities, including, but not limited to, research, manufacturing, distribution, pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee and independent contractor misconduct could also involve the improper use of individually identifiable information, including, without limitation, information obtained during clinical trials, which could result in regulatory sanctions and serious harm to our reputation. In addition, federal procurement laws impose substantial penalties for misconduct in connection with government contracts and require certain contractors to maintain a code of business ethics and conduct. It is not always possible to identify and deter employee and independent contractor misconduct, and any precautions we take to detect and prevent improper activities may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against us, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting or oversight obligations if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with the law and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate.

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

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

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

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

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

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

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

- the federal Physician Payments Sunshine Act, created under Section 6002 of Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, and its implementing regulations, which created annual reporting requirements for manufacturers of drugs, devices, biologicals and medical supplies for certain payments and “transfers of value” provided to

covered recipients, including physicians, as defined by such law, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or to adopt compliance programs as prescribed by state laws and regulations, or that otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and drug pricing; state and local laws requiring the licensure of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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

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

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

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

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

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

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access.

Other federal health reform measures have been proposed and adopted in the United States. For example, the Medicare Access and CHIP Reauthorization Act of 2015 ended the use of the statutory formula for clinician payment and established a quality payment incentive program, also referred to as the Quality Payment Program. This program provides clinicians with two ways to participate, including through the Advanced Alternative Payment Models, or APMs, and the Merit-based Incentive Payment System, or MIPS. In November 2019, CMS issued a final rule finalizing the changes to the Quality Payment Program. It is unclear how payment reductions or the introduction of the Quality Payment Program will impact overall physician reimbursement under the Medicare program. It is also unclear if changes in Medicare payments to providers would impact such providers' willingness to prescribe and administer our products, if approved.

Further, there has been heightened governmental scrutiny over the way companies set prices for their marketed products. For example, there have been several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and patient programs, and reform government program reimbursement methodologies for drug products.

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

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

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

There has been heightened governmental scrutiny in the United States and abroad of pharmaceutical pricing practices considering the rising cost of prescription drugs and biologics. In the United States, such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the former Trump Administration's budget proposal for fiscal year 2020 contained further drug price control measures that could be enacted during the 2020 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. The former Trump Administration also released a "Blueprint", or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of

pocket costs of drug products paid by consumers. HHS has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. On November 20, 2020, CMS issued an interim final rule through the CMS Innovation Center whereby Medicare Part B reimbursement for "certain high-cost prescriptions drugs" would be no more than most-favored-nation price (i.e., the lowest price) after adjustments, for a pharmaceutical product that the drug manufacturer sells in a member country of the Organization for Economic Cooperation and Development that has a comparable per-capita gross domestic product. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. While some of these and other measures may require additional authorization to become effective, members of Congress have and the new Biden Administration have indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Outside of the United States, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed.

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

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

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

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

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States and the United Kingdom, and authorities in the European Union, including applicable export control regulations, economic sanctions and embargoes on certain countries and persons, anti-money laundering laws, import and customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws.

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

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

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

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

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

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

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

and cost of tax compliance. We urge our stockholders to consult with their legal and tax advisors with respect to any such legislative changes and the potential tax consequences of investing in or holding our common stock.

Risks Related to Ownership of Our Common Stock

Innoviva, Inc. may exert a substantial influence on actions requiring stockholder vote, potentially in a manner that you do not support.

As of December 31, 2020, Innoviva, held approximately 51.0% of our issued and outstanding shares of common stock, and accordingly controls approximately 51.0% of our voting power. Innoviva's large ownership stake may allow it to exert a significant influence on actions requiring a stockholder vote, potentially including amendments to our certificate of incorporation, election of our board of directors, removal of any of our directors, adoption of measures that could delay or prevent a change in control or impede a merger, takeover, or other business combination involving us, and approval of other major corporate transactions. In addition, Innoviva's stock ownership may discourage a potential acquirer from making a tender offer or otherwise attempting to obtain control of us, which in turn could reduce our stock price or prevent our stockholders from realizing a premium over our stock price. Accordingly, our stockholders other than Innoviva may be unable to influence management and exercise control over our business.

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

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

- the commencement, enrollment or results of our planned and future clinical trials;
- the loss of any of our key scientific or management personnel;
- regulatory or legal developments in the United States and other countries;
- the success of competitive products or technologies;
- adverse actions taken by regulatory agencies with respect to our clinical trials or manufacturers;
- changes or developments in laws or regulations applicable to our product candidates and preclinical program;
- changes to our relationships with collaborators, manufacturers or suppliers;
- the results of our testing and clinical trials;
- unanticipated safety concerns;
- announcements concerning our competitors or the pharmaceutical industry in general;
- changes in the structure of healthcare payment systems;
- actual or anticipated fluctuations in our operating results;

- changes in our financial results, including our ability to continue as a going concern, or changes of recommendations by securities analysts;
- potential acquisitions;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates;
- the trading volume of our common stock on The Nasdaq Global Market;
- sales of our common stock by us, our executive officers and directors or our stockholders or the anticipation that such sales may occur in the future;
- general economic, political and market conditions and overall fluctuations in the financial markets in the United States or the United Kingdom;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry; and
- investors' general perception of us, our business and the antibiotic sector.

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

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

The issuance of additional shares of stock, or actual or perceived sales by large holders, could depress the market price of our common stock.

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

Our common stock is concentrated in several shareholders who hold large positions. For example, Innoviva, held 51.0% of our issued and outstanding common stock and AstraZeneca held 5.9% of our issued and outstanding common stock as of December 31, 2020. If holders of large numbers of our shares sell a substantial number of our shares of common stock in the public markets, or if there is the perception that such sales could occur, such sales could depress the market price of our shares of common stock and impair our ability to raise capital through the sale of additional equity securities. We cannot predict neither the number of shares that might be sold by our current or future

investors nor the effect that future sales of our shares of common stock would have on the market price of our shares of common stock.

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

Our executive officers, directors and current beneficial owners of 5% or more of our common stock and their respective affiliates beneficially own, in the aggregate, greater than 50% of our outstanding common stock, based on the number of shares of our common stock outstanding as of December 31, 2020. As a result, these persons, acting together, would be able to control all matters requiring stockholder approval, including the election and removal of directors, any merger, consolidation or sale of all or substantially all our assets, or other significant corporate transactions. The interests of this group of stockholders may not coincide with our interests or the interests of other stockholders. In addition, these persons, acting together, may have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership may harm the market price of our common stock by: delaying, deferring, or preventing a change in control; entrenching our management and/or the board of directors; impeding a merger, consolidation, takeover, or other business combination involving us; or by discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

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

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

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

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired more than 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

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

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

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

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

Under Section 107(b) of the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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

The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting.

Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

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

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

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

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

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

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

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

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

Pursuant to Section 404, we will be required to furnish a report by our senior management on our internal control over financial reporting. However, while we remain an EGC, we will not be required to include an attestation

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

General Risk Factors

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

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

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

There is no way of knowing with certainty whether we have experienced any data security incidents that have not been discovered. While we have no reason to believe this to be the case, attackers have become very sophisticated in the way they conceal access to systems, and many companies that have been attacked are not aware that they have been attacked. Any event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could disrupt our business, harm our reputation, compel us to comply with applicable federal and state breach notification laws and foreign law equivalents, subject us to time-consuming, distracting and expensive litigation, regulatory investigation and oversight, mandatory corrective action, require us to

verify the correctness of database contents, or otherwise subject us to liability under laws, regulations and contractual obligations, including those that protect the privacy and security of personal information. This could result in increased costs to us and result in significant legal and financial exposure and reputational harm. In addition, any failure or perceived failure by us or our vendors or business partners to comply with our privacy, confidentiality or data security-related legal or other obligations to third parties, or any further security incidents or other inappropriate access events that result in the unauthorized access, release or transfer of sensitive information, which could include personally identifiable information, may result in governmental investigations, enforcement actions, regulatory fines, litigation, or public statements against us by advocacy groups or others, and could cause third parties, including clinical sites, regulators or current and potential partners, to lose trust in us, or we could be subject to claims by third parties that we have breached our privacy- or confidentiality-related obligations. Moreover, data security incidents and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security, measures intended to protect our information technology systems and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or security incidents.

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

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

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

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

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

liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our principal offices occupy 20,062 square feet of leased office, research and development and laboratory facility space in Waltham, Massachusetts, pursuant to a lease agreement that expires in December 2022. We believe that our current facilities are suitable to meet our current needs.

Item 3. Legal Proceedings

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

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information

Our common stock is traded on The Nasdaq Global Market under the symbol "ETTX."

Holders of Record

As of March 17, 2021, we had approximately 23 holders of record of our common stock. Certain shares are held in "street" name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

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

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

Recent Sales of Unregistered Equity Securities

On June 11, 2020, we completed a private placement transaction, the First Private Placement, in which we sold to Innoviva a total of 14,000,000 shares of our common stock and issued warrants to purchase an additional 14,000,000 shares of our common stock, with an exercise price per share of $2.50. The First Private Placement was closed in two tranches for total aggregate gross proceeds of $35.0 million.

On September 1, 2020, we completed a private placement transaction pursuant to a securities purchase agreement with the purchasers named therein, or the Investors, in which we sold to the Investors a total of 8,183,878 shares of our common stock, issued warrants to purchase an additional 9,345,794 shares of our common stock, with an exercise price per share of $2.675, and issued pre-funded warrants to purchase an additional 1,161,916 shares of our common stock, with an exercise price per share of $0.001, collectively, the Second Private Placement. The Second Private Placement resulted in total aggregate gross proceeds of approximately $25.0 million.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. Selected Financial Data

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

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

You should read the following information in conjunction with the consolidated financial information and the notes thereto appearing elsewhere in this Annual Report on Form 10-K. In addition, you should read the "Risk Factors" and "Special Note Regarding Forward-Looking Statements" in this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are an advanced, clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of targeted antibacterial products that address high unmet medical needs to treat serious infections caused by multidrug-resistant pathogens.

Our lead product candidate, SUL-DUR, is an IV combination of sulbactam, an IV β-lactam antibiotic, and durlobactam, a novel broad-spectrum IV BLI, that we are developing for the treatment of pneumonia and bloodstream infections caused by carbapenem-resistant *Acinetobacter baumannii*, or *Acinetobacter*. Based on current carbapenem resistance rates, we estimate there are in excess of 200,000 hospital-treated carbapenem-resistant *Acinetobacter* infections annually across the United States, Europe, the Middle East and China for which significant morbidity and mortality exists due to limited treatment options. We initiated ATTACK (***A****cinetobacter* **T**reatment **T**rial **A**gainst **C**olistin), our single Phase 3 registration trial in April 2019, with top-line data readout expected in the second half of 2021. ATTACK is a global, multi-center trial that will evaluate approximately 120 patients with confirmed carbapenem-resistant *Acinetobacter* hospital-acquired pneumonia, ventilator-acquired pneumonia, ventilated pneumonia or bloodstream infections, or a combination of these. We believe that the data from the ATTACK trial, data from our other clinical trials of SUL-DUR and non-clinical data will be sufficient to submit an NDA to the FDA.

Our second late-stage product candidate, zoliflodacin, is a novel orally administered molecule being developed for the treatment of uncomplicated gonorrhea. The bacterial pathogen responsible for gonorrhea is *N. gonorrhoeae*, including multidrug-resistant strains. Intramuscular injection of ceftriaxone now represents the only CDC recommended treatment option for the estimated 1.6 million annual cases of gonorrhea in the United States. We believe there is a growing unmet need for a single-dose oral antibiotic that will reliably treat patients with gonorrhea, including infections

caused by multidrug-resistant strains of *N. gonorrhoeae*, which are emerging globally. The Phase 3 registration trial, initiated in September 2019, is a multi-center, open-label, noninferiority trial in approximately 1,000 enrolled patients with uncomplicated gonorrhea. Our nonprofit collaborator, GARDP, is the sponsor of the registration trial and is responsible for all trial expenses. We believe data from the Phase 3 registration trial, along with data from our other clinical trials of zoliflodacin and non-clinical data will be sufficient for submitting an NDA to the FDA.

We are also developing ETX0282CPDP for the treatment of complicated urinary tract infections, or cUTIs, including those caused by multidrug-resistant *Enterobacteriaceae*. ETX0282CPDP is an oral combination of ETX0282 with cefpodoxime proxetil. We believe there is a significant unmet need for new oral antibiotics to reliably treat the estimated 3 to 4 million patients diagnosed annually with cUTIs. We have reported preliminary Phase 1 trial results, and subsequently demonstrated that an extended release tablet formulation achieved preclinical proof-of-concept of the desired pharmacokinetic profile both in vitro and in non-human primates. Having successfully completed the initial Phase 1 studies and preclinical work to deliver a formulation with the desired extended release profile, we are currently prioritizing our resources on completing the ATTACK trial and supporting the ongoing Phase 3 registration trial for zoliflodacin, while we evaluate options for further clinical development of ETX0282CPDP.

Lastly, we are advancing development of a novel class of antibiotics, NBPs. We believe NBPs constitute a potential new class of Gram-negative antibacterial agents that are designed to target a broad spectrum of multidrug resistant bacterial pathogens that overcome the main source of β-lactam resistance which is driven by β-lactamase activity. This novel class of agent is designed to target a broad spectrum of multidrug resistant bacterial pathogens that are part of the CDC/World Health Organization, or WHO, list of high unmet medical need or ESKAPE pathogens. We selected ETX0462 as the initial clinical candidate for this program, based on demonstrated activity against *Pseudomonas* and a number of high-priority biothreat pathogens combined with a strong preclinical safety profile and attractive physiochemical properties. We are currently working to complete the required pre-clinical activities by early 2022 to enable the program to advance into a Phase 1 clinical trial.

Since our inception in May 2015, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, discovering product candidates and securing related intellectual property rights, conducting discovery and development activities for our programs and planning for potential commercialization. We do not have any products approved for sale and have not generated any revenue from product sales. As of December 31, 2020, we have funded our operations primarily with net cash proceeds of $104.2 million from the sale of our preferred stock, net cash proceeds of $65.6 million from the sale of common stock in our initial public offering, and net cash proceeds of $57.9 million from the sale of common stock, warrants and pre-funded warrants in private placements to certain investors in 2020. 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 DOD, and we have received non-profit awards from GARDP and upfront and milestone payments from our license and collaboration agreement with Zai Lab.

Funding Arrangements

NIH

In June 2020, we entered into a contract with NIAID, part of the NIH, with an effective date of July 1, 2020. The contract consists of an initial award of approximately $3.0 million, with the potential to increase up to $15.5 million, will be used to develop novel molecules from our NBP platform. Funding from the contract will support research towards developing molecules with expanded Gram-negative spectrum against antibiotic-resistant bacterial pathogens including *E. coli*, *Acinetobacter*, *Pseudomonas* and *Klebsiella*. Through December 31, 2020, we had received $0.6 million in payments and we had recorded $1.3 million of income under this funding arrangement.

CARB-X

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 our ETX0282CPDP and ETX0462 programs. These funding arrangements could cover up to $18.2 million of our specified research expenditures

from April 2017 through September 2021. Through December 31, 2020, we had received $9.5 million in payments and we have recorded $10.3 million of grant income under these funding arrangements.

License and Collaboration Agreements

GARDP

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

Zai Lab

In April 2018, we entered into a license and collaboration agreement with Zai Lab pursuant to which Zai Lab licensed exclusive rights to durlobactam and SUL-DUR in the Asia-Pacific region. Under the terms of the agreement, Zai Lab will fund most of our registration trial costs in China for SUL-DUR, including all costs in China for our Phase 3 registration trial of SUL-DUR, with the exception of Phase 3 patient drug supply of licensed product. As of December 31, 2020, we have received net payments of $14.7 million, representing the $5.0 million upfront payment, $7.0 million of milestone payments, $0.6 million of research support payments and $4.2 million of certain other reimbursable registration trial costs, less applicable taxes of $2.1 million, from Zai Lab and we have recognized revenue of $12.0 million under this agreement.

Components of Results of Operations

Revenue

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

Operating Expenses

Research and Development Expenses

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

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

- costs related to compliance with regulatory requirements; and
- facilities-related expenses, which include allocated rent and maintenance of facilities and other operating costs.

Costs associated with research and development activities are expensed as incurred. Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or other information provided to us by our vendors. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered, or the services rendered.

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

To date, substantially all of our research and development expenses have been related to the preclinical and clinical development of our product candidates and preclinical program. The following table shows our research and development expenses by development program and type of activity for the years ended December 31, 2020 and 2019:

	Year Ended December 31,	
	2020	2019
Direct research and development expenses by program:		
SUL-DUR	$ 23,356	$ 24,005
Zoliflodacin	2	67
ETX0282CPDP	160	1,573
ETX0462	1,968	1,561
Other preclinical programs	822	849
Unallocated research and development expenses:		
Personnel related (including stock-based compensation)	12,383	9,767
Facilities, supplies and other	2,331	2,344
Total research and development expenses	$ 41,022	$ 40,166

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. 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 impact of COVID-19 on hospitals participating in the trials and their ability to focus on and direct resources to our trials;

- the number of trials required for approval and any requirement for extension trials;
- per-patient trial costs;
- the number of patients that participate in the trials;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- the duration of patient follow-up; and
- the efficacy and safety profiles of the product candidates.

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

General and Administrative Expenses

General and administrative expenses consist of salaries and benefits and stock-based compensation expense for personnel in executive, finance and administrative functions. General and administrative costs also include facilities-related costs not otherwise included in research and development expenses and professional fees for legal, patent, consulting, insurance, 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, development and commercialization activities of our product candidates. Additionally, if and when we believe a regulatory approval of a product candidate appears likely, we anticipate an increase in payroll and other employee-related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing functions for that product candidate.

Other Income

Grant Income

Grant income consists of income recognized in connection with grants we received under our funding arrangements with the Trustees of Boston University through the CARB-X program, as well as amounts received under our NIH contract. Grant income is recognized in the period during which the related specified expenses are incurred.

Interest Income

Interest income consists of interest earned on our cash and investment balances, which are primarily held in money market funds and U.S. Treasury Securities.

Provision for Income Taxes

The provision for income taxes primarily consists of provisions for foreign withholding income taxes on payments related to our agreement with Zai Lab.

Results of Operations

Years Ended December 31, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019:

	Year Ended December 31,		
	2020	2019	$ Change
	(in thousands)		
Revenue	$ —	$ 7,000	$ (7,000)
Operating expenses:			
Research and development	41,022	40,166	856
General and administrative	13,209	13,770	(561)
Total operating expenses	54,231	53,936	295
Loss from operations	(54,231)	(46,936)	(7,295)
Other income:			
Grant income	3,562	2,300	1,262
Interest income	173	1,463	(1,290)
Total other income	3,735	3,763	(28)
Loss before income taxes	(50,496)	(43,173)	(7,323)
Provision for income taxes	—	677	(677)
Net loss	$ (50,496)	$ (43,850)	$ (6,646)

Revenue

We recognized no revenue for the year ended December 31, 2020, compared to $7.0 million for the year ended December 31, 2019. The decrease of $7.0 million was due to the timing of milestones achieved pursuant to the collaboration agreement with Zai Lab, which we entered into in April 2018.

Research and Development Expenses

Research and development expenses were $41.0 million for the year ended December 31, 2020, compared to $40.2 million for the year ended December 31, 2019. The increase of $0.9 million was primarily due to an increase of $2.6 million in personnel expenses associated with higher headcount, higher salaries and higher stock-based compensation expense resulting from options and restricted stock units granted during the year ended December 31, 2020; offset in part by a decrease of $1.4 million in preclinical and clinical development expenses related to the

advancement of our ETX0282CPDP product candidate and a decrease of $0.6 million in clinical development expenses related to the advancement of our SUL-DUR product candidate. The decrease in preclinical and clinical development expenses of $1.4 million associated with the advancement of ETX0282CPDP was primarily due to a decrease of $1.7 million in clinical trial costs, partially offset by increases of $0.2 million in other preclinical expenses and $0.1 million in drug manufacturing costs. The decrease in clinical development expenses of $0.6 million associated with the advancement of our SUL-DUR product candidate was primarily due to a decrease of $1.2 million in clinical trial costs and a decrease of $0.4 million in drug manufacturing costs; partially offset by an increase of $0.5 million in NDA filing support and an increase of $0.5 million in commercial readiness activities.

General and Administrative Expenses

General and administrative expenses were $13.2 million for the year ended December 31, 2020, compared to $13.8 million for the year ended December 31, 2019. The decrease of $0.6 million was driven by a decrease of $0.7 million in consulting expenses, a decrease of $0.6 million in VAT and other taxes, and a decrease of $0.5 million in legal expenses. These decreases were partially offset by an increase of $0.6 million in insurance premiums and an increase of $0.5 million in personnel expenses associated with higher headcount and higher salaries.

Other Income

Other income was $3.7 million for the year ended December 31, 2020, compared to $3.8 million for the year ended December 31, 2019. The decrease of approximately $29,000 was due to a decrease in interest income of $1.3 million, offset by an increase of $1.3 million in grant income associated with our agreements with CARB-X and NIH.

Provision for Income Taxes

There was no provision for income taxes for the year ended December 31, 2020, compared to $0.7 million for the year ended December 31, 2019. The $0.7 million decrease was due to the timing of milestone payments received in connection with our ongoing license and collaboration agreement with Zai Lab. Our losses before income taxes were generated in the United States and United Kingdom. Consistent with all prior periods, we did not record any income tax benefit for its operating losses due to the uncertainty regarding future taxable income. Accordingly, a full valuation allowance has been established against the deferred tax assets as of December 31, 2020.

Liquidity and Capital Resources

Overview

As of December 31, 2020, we had cash and cash equivalents of $53.2 million. We have funded our operations to date with the proceeds from offerings of our securities, including $104.2 million from the sale of redeemable convertible preferred stock, $65.6 million from the sale of common stock in our initial public offering and $57.9 million from the sale of common stock and warrants in private placements to certain investors during the year ended December 31, 2020. In addition, we also have received funding or financial commitments from, or have had our program activities conducted and funded by, the U.S. government through arrangements with NIAID, CARB-X, NIH and the DOD, and have received non-profit awards from GARDP and upfront and milestone payments from Zai Lab.

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 $50.5 million for the year ended December 31, 2020. As of December 31, 2020, we had an accumulated deficit of $184.5 million.

We believe that our existing cash and cash equivalents, will enable us to fund our operating expenses and capital requirements through the first quarter of 2022. 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:

- the unpredictable duration and economic impact of the COVID-19 pandemic;
- successful enrollment in, and completion of clinical trials;
- performing preclinical studies and clinical trials in compliance with requirements of the FDA, the EMA, or any comparable regulatory authority;
- the ability of collaborators to manufacture sufficient quantity of product for development, clinical trials or potential commercialization;
- obtaining marketing approvals with labeling for sufficiently broad patient populations and indications, without unduly restrictive distribution limitations or safety warnings, such as black box warnings or a risk evaluation and mitigation strategies program;
- obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third parties for manufacturing capabilities;
- launching commercial sales of products, if and when approved, whether alone or in collaboration with others;
- acceptance of the therapies, if and when approved, by physicians, patients and third-party payors;
- competing effectively with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- protecting our rights in our intellectual property portfolio; and
- maintaining a continued acceptable safety profile of our drugs following approval.

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

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

As a result, we will need substantial additional funding to support our continuing operations and to pursue our growth strategy. Until such time, if ever, when we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaboration, license and development agreements. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to a third party to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our failure to raise capital as and when needed would compromise our ability to pursue our business strategy.

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

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

Aspire Common Stock Purchase Agreement

In October 2019, we entered into a common stock purchase agreement, or CSPA, with Aspire Capital Fund, LLC, or Aspire, which provides that, upon the terms and subject to the conditions and limitations set forth therein, Aspire is committed to purchase up to an aggregate of $20.0 million of shares of our common stock over the 30-month term of the CSPA. Under the CSPA, on any trading day selected by us on which the closing price of our common stock is equal to or greater than $0.25 per share, we have the right, in our sole discretion, to present Aspire with a purchase notice directing Aspire to purchase up to 50,000 shares of our common stock per business day, at a purchase price equal to the lesser of the lowest sale price of common stock on the purchase date, or the arithmetic average of the three lowest closing sale prices during the 10 consecutive business days ending on the trading day immediately preceding the purchase date. We and Aspire also may mutually agree to increase the number of shares that may be sold to as much as 2,000,000 shares per business day.

We control the timing and amount of any sales to Aspire, and we are not limited with respect to use of proceeds or by any financial or business covenants, restrictions on future financings, rights of first refusal, participation rights, penalties or liquidated damages in the CSPA. The CSPA further provides that the number of shares that may be sold pursuant to the CSPA will be limited to 2,626,165 shares, which represented 19.99% of our outstanding shares of common stock as of October 21, 2019, unless stockholder approval is obtained to issue more than 19.99%. During the year ended December 31, 2020, no shares were purchased by Aspire pursuant to the CSPA.

Cash Flows

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

	Year Ended December 31,	
	2020	2019
Net cash used in operating activities	$ (45,426)	$ (44,743)
Net cash provided by investing activities	24,982	11,360
Net cash provided by financing activities	57,657	57
Net increase (decrease) in cash and cash equivalents	$ 37,213	$ (33,326)

Operating Activities

During the year ended December 31, 2020, operating activities used $45.4 million of cash, resulting from our net loss of $50.5 million partially offset by non-cash charges of $3.1 million and net cash provided by changes in operating assets and liabilities of $2.0 million. Net cash provided by changes in operating assets and liabilities for the year ended December 31, 2020 consisted primarily of a $1.9 million decrease in other assets, a $1.0 million increase in accrued expenses and other liabilities, and a $0.4 million decrease in prepaid expenses. These were partially offset by a $0.7 million increase in grants receivable and a $0.6 million decrease in accounts payable.

During the year ended December 31, 2019, operating activities used $44.7 million of cash, resulting from our net loss of $43.9 million and net cash used for changes in operating assets and liabilities of $2.8 million, partially offset by non-cash charges of $1.9 million. Net cash used for changes in operating assets and liabilities for the year ended December 31, 2019 consisted primarily of a $3.2 million increase in prepaid expenses, a $2.7 million increase in other current assets and a $0.2 million decrease in deferred rent. These were partially offset by a $2.9 million increase in accrued expenses and other liabilities and a $0.5 million decrease in grants receivable.

Investing Activities

During the year ended December 31, 2020, net cash provided by investing activities was $25.0 million, consisting primarily of proceeds from maturities of short-term investments.

During the year ended December 31, 2019, net cash provided by investing activities was $11.4 million, consisting of proceeds from maturities of short-term investments of $56.4 million, offset by purchases of short-term investments of $45.0 million.

Financing Activities

During the year ended December 31, 2020, net cash provided by financing activities was $57.7 million, which consisted of proceeds from the issuance of common stock and warrants in the First Private Placement and Second Private Placement, net of issuance costs.

During the year ended December 31, 2019, net cash provided by financing activities was $0.1 million, which consisted of $0.2 million of proceeds from the sale of shares of our common stock under our CPSA with Aspire and $0.1 million of proceeds from stock option exercises, partially offset by $0.2 million of payments of initial public offering costs.

Contractual Obligations and Commitments

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

Off-Balance Sheet Arrangements

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

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues 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 , *Summary of Significant Accounting Policies*, in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition

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

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

As part of the accounting for these arrangements, we may be required to use significant judgment to determine: (a) the performance obligations in the contract under step (ii) above, (b) the transaction price under step (iii) above and (c) the timing of revenue recognition, including the appropriate measure of progress in step (v) above. We use judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price, as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. If a milestone or other variable consideration relates specifically to our efforts to satisfy a single performance obligation or to a specific outcome from satisfying the performance obligation, we generally allocate

the milestone amount entirely to that performance obligation once it is probable that a significant revenue reversal would not occur.

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

Licenses of intellectual property

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

Customer options

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

Milestone payments

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

Research and Development Expenses

All research and development expenses are expensed as incurred. Research and development expenses comprise costs incurred in performing research and development activities, including compensation, benefits and other employee costs; equity-based compensation expense; laboratory and clinical supplies and other direct expenses; facilities expenses; overhead expenses; fees for contractual services, including preclinical studies, clinical trials, clinical manufacturing and raw materials; and other external expenses. Nonrefundable advance payments for research and development activities are capitalized and expensed over the related service period or as goods are received. When third-

party service providers' billing terms do not coincide with our period-end, we are required to make estimates of our obligations to those third parties, including clinical trial costs, contractual service costs and costs for supply of our drug candidates, incurred in a given accounting period and record accruals at the end of the period. We base our estimates on our knowledge of the research and development programs, services performed for the period and the expected duration of the third-party service contract, where applicable.

Recent Accounting Pronouncements

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

Emerging Growth Company Status

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

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

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

Item 8. Financial Statements and Supplementary Data

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

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2020. Based on the evaluation of our disclosure controls and procedures as of December 31, 2020, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at a reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) and 15d-15(f) under the Exchange Act.

Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in "Internal Control-Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO. Based on this assessment, management concluded that, as of December 31, 2020, our internal control over financial reporting was effective based on criteria established in the COSO 2013 framework.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm on internal control over financial reporting due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal Control over Financial Reporting

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

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers, and Corporate Governance

The information required by this item will be included in the information set forth in the sections titled "Proposal 1 – Election of Directors," "Executive Officers," and "Information Regarding the Board and Corporate Governance" and "Delinquent Section 16(a) Reports," if applicable, in our definitive proxy statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders, or our Proxy Statement, and is incorporated by reference.

Item 11. Executive Compensation

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

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

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

Item 13. Certain Relationships and Related Transactions and Director Independence

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

Item 14. Principal Accounting Fees and Services

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

PART IV

Item 15. Exhibits, Financial Statements Schedules

(a)(1) Financial Statements.

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

(a)(2) Financial Statement Schedules.

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

(a)(3) Exhibits.

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

Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Company (incorporated herein by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on September 28, 2018).
3.1.1	Certificate of Amendment to the Amended and Restated Certificate of Incorporation of the Company (incorporated herein by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on June 11, 2020).
3.2	Amended and Restated Bylaws of the Company (incorporated herein by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on September 28, 2018).
4.1	Form of Common Stock Certificate of the Company (incorporated herein by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
4.2	Registration Rights Agreement, by and between the Company and Aspire Capital Fund, LLC, dated October 21, 2019 (incorporated herein by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on October 21, 2019).

4.3	Description of the Registrant's Company's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934 (incorporated herein by reference to Exhibit 4.3 to the Company's Annual Report on Form 10-K (File No. 001-38670) filed with the SEC on March 11, 2020).
4.4	Registration Rights Agreement, by and between the Company and Innoviva, Inc., dated April 22, 2020 (incorporated herein by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on April 22, 2020).
4.5	Form of Warrant Certificate (incorporated herein by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on April 13, 2020).
4.6	Registration Rights Agreement, by and between the Company and the Investors named therein, dated September 1, 2020 (incorporated herein by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on September 1, 2020).
4.7	Form of Common Stock Purchase Warrant (incorporated herein by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on September 1, 2020).
4.8	Form of Pre-Funded Common Stock Purchase Warrant (incorporated herein by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on September 1, 2020).
10.1+	Form of Indemnification Agreement by and between the Company and each of its directors and officers (incorporated herein by reference to Exhibit 10.16 to the Company's Registration Statement on Form S-1/A (File No. 333-226920), filed with the SEC on September 18, 2018).
10.2	Common Stock Purchase Agreement, by and between the Company and Aspire Capital Fund, LLC, dated October 21, 2019 (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on October 21, 2019).
10.3+	Forms of Stock Option Grant Notice and Stock Option Agreement under the 2018 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.4+	2018 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q (File No. 001-38670), filed with the SEC on November 14, 2018).
10.5+	Amended and Restated Stock Incentive Plan (incorporated herein by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.6+	Form of Nonqualified Stock Option Agreement (Senior Management) under the Amended and Restated Stock Incentive Plan (incorporated herein by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.7+	Form of Incentive Stock Option Agreement (Senior Management) under the Amended and Restated Stock Incentive Plan (incorporated herein by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).

10.8+	Employment Agreement between the Company and Manoussos Perros, effective September 25, 2018 (incorporated herein by reference to Exhibit 10.13 to the Company's Registration Statement on Form S-1/A (File No. 333-226920), filed with the SEC on September 18, 2018).
10.9+	Employment Agreement between the Company and Michael Gutch, effective September 25, 2018 (incorporated herein by reference to Exhibit 10.14 to the Company's Registration Statement on Form S-1/A (File No. 333-226920), filed with the SEC on September 18, 2018).
10.10+	Employment Agreement between the Company and Ruben Tommasi, effective September 25, 2018 (incorporated herein by reference to Exhibit 10.12 to the Company's Annual Report on Form 10-K (File No. 001-38670), filed with the SEC on March 29, 2019).
10.11†	Amended and Restated Business Transfer and Subscription Agreement, dated March 29, 2016, by and among AstraZeneca AB, AstraZeneca UK Limited, AstraZeneca Pharmaceuticals LP, and the Company (incorporated herein by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.12†	Amendment to Amended and Restated Business Transfer and Subscription Agreement, dated August 28, 2017, by and among AstraZeneca AB, AstraZeneca UK Limited, AstraZeneca Pharmaceuticals LP, and the Company (incorporated herein by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.13†	Amendment No. 2 to Amended and Restated Business Transfer and Subscription Agreement, dated January 30, 2018, by and among AstraZeneca AB, AstraZeneca UK Limited, AstraZeneca Pharmaceuticals LP, and the Company (incorporated herein by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.14†	Collaboration Agreement, dated July 4, 2017, by and between the Drugs for Neglected Diseases initiative, acting through the Global Antibiotic Research and Development Partnership, and the Company (incorporated herein by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.15	Novation of Contract, dated January 11, 2019, by and between the Global Antibiotic Research and Development Partnership and the Company (incorporated herein by reference to Exhibit 10.17 to the Company's Annual Report on Form 10-K (File No. 001-38670), filed with the SEC on March 29, 2019).
10.16†	License and Collaboration Agreement, dated April 25, 2018, by and between Zai Lab (Shanghai) Co., Ltd. and the Company (incorporated herein by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.17+	Amended Non-Employee Director Compensation Policy, as amended December 6, 2019 (incorporated herein by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (File No. 001-38670), filed with the SEC on August 6, 2020).
10.18+	Special Bonus Award Memorandum, dated May 15, 2020 (incorporated herein by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q (File No. 001-38670), filed with the SEC on August 6, 2020).

10.19	Securities Purchase Agreement, by and between the Company and Innoviva, Inc., dated April 12, 2020 (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on April 13, 2020).
10.20	Form of Voting Agreement (incorporated herein by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on April 13, 2020).
10.21	Investor Rights Agreement, by and between the Company and Innoviva, Inc., dated April 22, 2020 (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on April 22, 2020).
10.22+	First Amendment to 2018 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q (File No. 001-38670), filed with the SEC on August 6, 2020).
10.23	Securities Purchase Agreement, by and between the Company and the Investors named therein, dated August 27, 2020 (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on September 1, 2020).
10.24+	Form of Restricted Stock Unit Grant Notice (Time-Based) (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on November 6, 2020).
10.25+	Form of Restricted Stock Unit Grant Notice (Performance-Based) (incorporated herein by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on November 6, 2020).
10.26+	Form of Restricted Stock Unit Grant Agreement (incorporated herein by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on November 6, 2020).
10.27+	Form of Executive Officer Employment Agreement (incorporated herein by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (File No. 001-38670), filed with the SEC on May 7, 2020).
21.1	Subsidiaries of Entasis Therapeutics Holdings Inc.
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on the signature page to this report).
31.1	Certification of Chief Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Chief Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Chief Executive Officer and Chief Financial Officer Pursuant to 18 U.S.C. Section 1350, as adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

101.INS	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	The cover page from the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020 formatted in inline XBRL (included in Exhibit 101).

---

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

\+ Indicates a management contract or compensatory plan.

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

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 and 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

ENTASIS THERAPEUTICS HOLDINGS INC.

Date: March 23, 2021

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

POWER OF ATTORNEY

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

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

Signature	Title	Date
/s/ Manoussos Perros Manoussos Perros, Ph.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 23, 2021
/s/ Michael Gutch Michael Gutch, Ph.D.	Chief Business Officer and Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 23, 2021
/s/ David Meek David Meek	Chairman of the Board	March 23, 2021
/s/ Heather Behanna Heather Behanna, Ph.D.	Director	March 23, 2021
/s/ David C. Hastings David C. Hastings	Director	March 23, 2021
/s/ Heather Preston Heather Preston, M.D.	Director	March 23, 2021
/s/ Howard Mayer Howard Mayer, M.D.	Director	March 23, 2021

ENTASIS THERAPEUTICS HOLDINGS INC.
Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

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

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Entasis Therapeutics Holdings Inc. and subsidiaries (the Company) as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for the years then ended, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ KPMG LLP

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

Boston, Massachusetts
March 23, 2021

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

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 53,247	$ 16,034
Short-term investments	—	24,962
Grants receivable	1,890	1,232
Prepaid expenses	4,160	4,560
Other current assets	835	2,218
Total current assets	60,132	49,006
Property and equipment, net	222	345
Operating lease right-of-use assets	1,141	1,620
Other assets	63	63
Total assets	$ 61,558	$ 51,034
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 660	$ 1,304
Accrued expenses and other current liabilities	7,905	6,252
Total current liabilities	8,565	7,556
Operating lease liabilities, net of current portion	704	1,321
Total liabilities	9,269	8,877
Commitments (Notes 6 and 14)		
Stockholders' equity:		
Common stock, par value $0.001; 125,000,000 shares authorized and 36,637,357 and 13,291,563 shares issued and outstanding as of December 31, 2020 and 2019, respectively	37	13
Additional paid-in capital	236,707	176,103
Accumulated deficit	(184,455)	(133,959)
Total stockholders' equity	52,289	42,157
Total liabilities and stockholders' equity	$ 61,558	$ 51,034

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

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

	Year Ended December 31,	
	2020	2019
Revenue	$ —	$ 7,000
Operating expenses:		
Research and development	41,022	40,166
General and administrative	13,209	13,770
Total operating expenses	54,231	53,936
Loss from operations	(54,231)	(46,936)
Other income:		
Grant income	3,562	2,300
Interest income	173	1,463
Total other income	3,735	3,763
Loss before income taxes	(50,496)	(43,173)
Provision for income taxes	—	677
Net loss	(50,496)	(43,850)
Net loss per share —basic and diluted	$ (2.10)	$ (3.33)
Weighted average common stock outstanding—basic and diluted	24,060,615	13,160,357

	Year Ended December 31,	
	2020	2019
Other comprehensive loss:		
Net loss	$ (50,496)	$ (43,850)
Net unrealized gain on investments held	—	9
Comprehensive loss	$ (50,496)	$ (43,841)

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

ENTASIS THERAPEUTICS HOLDINGS INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balances as of December 31, 2018	13,124,842	$ 13	$ 172,988	$ (9)	$ (90,109)	$ 82,883
Stock-based compensation expense	—	—	2,421	—	—	2,421
Exercise of stock options	12,554	—	52	—	—	52
Sale of common stock, net of issuance costs of $284	50,000	—	—	—	—	—
Issuance of commitment shares in connection with Aspire Common Stock Purchase Agreement	104,167	—	642	—	—	642
Unrealized gain on investments held	—	—	—	9	—	9
Net loss	—	—	—	—	(43,850)	(43,850)
Balances as of December 31, 2019	13,291,563	13	176,103	—	(133,959)	42,157
Stock-based compensation expense	—	—	2,951	—	—	2,951
Sale of common stock and warrants in private placements, net of issuance costs	22,183,878	22	57,653	—	—	57,675
Exercise of warrants	1,161,916	2	—	—	—	2
Net loss	—	—	—	—	(50,496)	(50,496)
Balances as of December 31, 2020	36,637,357	$ 37	$ 236,707	$ —	$ (184,455)	$ 52,289

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

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

	Year Ended December 31,	
	2020	2019
Cash flows from operating activities:		
Net loss	$ (50,496)	$ (43,850)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	141	142
Stock-based compensation expense	2,951	2,421
Amortization and accretion of investments	(37)	(686)
Changes in operating assets and liabilities:		
Grants receivable	(658)	474
Prepaid expenses	400	(3,206)
Other assets	1,881	(2,711)
Accounts payable	(644)	(30)
Accrued expenses and other liabilities	1,036	2,878
Deferred rent	—	(175)
Net cash used in operating activities	(45,426)	(44,743)
Cash flows from investing activities:		
Purchases of property and equipment	(18)	(105)
Proceeds from maturities of short-term investments	25,000	56,415
Purchases of short-term investments	—	(44,950)
Net cash provided by investing activities	24,982	11,360
Cash flows from financing activities:		
Proceeds from the issuance of common stock and warrants in private placements, net	57,657	155
Proceeds from exercise of stock options	—	52
Payments of initial public offering costs	—	(150)
Net cash provided by financing activities	57,657	57
Net increase (decrease) in cash and cash equivalents	37,213	(33,326)
Cash and cash equivalents at beginning of the year	16,034	49,360
Cash and cash equivalents at end of the year	$ 53,247	$ 16,034
Supplemental disclosure of non-cash investing and financing activities:		
Commitment shares issued in connection with common stock purchase agreement	$ —	$ 642
Supplemental disclosure of cash flow information:		
Cash paid for taxes	$ —	$ 677

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

ENTASIS THERAPEUTICS HOLDINGS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Description of Business

Entasis Therapeutics Holdings Inc., or Entasis, or the Company, is an advanced, clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of targeted antibacterial products that address high unmet medical needs to treat serious infections caused by multidrug-resistant pathogens. The Company has four subsidiaries: Entasis Therapeutics Limited; Entasis Therapeutics Inc.; Entasis Therapeutics Security Corporation; and Entasis Therapeutics (Ireland) Limited.

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

On April 12, 2020, the Company entered into a securities purchase agreement, or the First Securities Purchase Agreement, with Innoviva Inc., or Innoviva, pursuant to which the Company issued and sold to Innoviva, in a private placement, 14,000,000 newly issued shares of common stock of the Company at $2.50 per share, and warrants to purchase up to 14,000,000 shares of common stock with an exercise price per share of $2.50, resulting in an aggregate gross purchase price of approximately $35.0 million, collectively, the First Private Placement. As a result of the transaction, Innoviva acquired control of the Company, owning approximately 51.3% of the Company's common stock without giving effect to the potential exercise of its warrants.

On August 27, 2020, the Company entered into another securities purchase agreement, or the Second Securities Purchase Agreement, with the purchasers named therein, or the Investors, which included existing stockholder Innoviva. Pursuant to the Second Securities Purchase Agreement, the Company issued and sold to the Investors in a private placement (i) 8,183,878 newly issued shares of common stock of the Company at $2.675 per share, (ii) warrants to purchase an aggregate of 9,345,794 shares of common stock with an exercise price of $2.675, and (iii) pre-funded warrants, in lieu of common stock, to purchase an aggregate of 1,161,916 shares of common stock with an exercise price of $0.001 per share, resulting in aggregate gross proceeds of approximately $25.0 million, which is referred to collectively as the Second Private Placement. The closing of the Second Private Placement occurred on September 1, 2020. As a result of the transaction, Innoviva owned approximately 52.6% of the Company's common stock without giving effect to the potential exercise of its warrants.

Risks and Uncertainties

As of December 31, 2020, the Company had $53.2 million in cash and cash equivalents, and an accumulated deficit of $184.5 million. Since its inception through December 31, 2020, the Company has funded its operations primarily with proceeds from the sale of preferred stock, common stock, warrants and pre-funded warrants. The Company also has either directly received funding or financial commitments from, or has had its program activities conducted and funded by, United States government agencies, non-profit entities and the collaboration agreement with Zai Lab (Shanghai), Co., Ltd., or Zai Lab. In the absence of positive cash flows from operations, the Company is highly dependent on its ability to find additional sources of funding in the form of debt, equity financing, strategic collaborations, or partnerships. If the Company raises additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, it may be required to relinquish valuable rights to its technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable. If the Company is unable to raise additional funds through equity or debt financings when needed, it may be required to delay, limit, reduce or terminate drug development or future commercialization efforts or grant rights to a third party to develop and market product candidates. The Company's failure to raise capital as and when needed would compromise its ability to pursue its business strategy. The Company believes its existing cash and cash equivalents will enable it to fund its operating expenses and capital requirements through the end of the first quarter of 2022.

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

As a clinical-stage company, Entasis is subject to a number of risks common to other life science companies, including, but not limited to, raising additional capital, development by its competitors of new technological innovations, risk of failure in preclinical and clinical studies, safety and efficacy of its product candidates in clinical trials, the risk of relying on external parties such as contract research organizations and contract manufacturing organizations, the regulatory approval process, market acceptance of the Company's products once approved, lack of marketing and sales history, dependence on key personnel and protection of proprietary technology. The Company's therapeutic programs are currently pre-commercial, spanning discovery through late-stage development and will require additional research and development efforts, including the completion of Phase 3 registration trials and regulatory approval, prior to commercialization of any product candidates. These efforts require significant amounts of additional capital, adequate personnel, infrastructure, and extensive compliance-reporting capabilities. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained, that any products developed will obtain necessary regulatory approval or that any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate revenue from product sales. The Company may never achieve profitability, and unless and until it does, it will continue to need to raise additional capital or obtain financing from other sources, such as strategic collaborations or partnerships.

The COVID-19 pandemic has, and will likely continue to have, a significant impact on the U.S. economy and businesses. The social distancing and stay-at-home orders issued by national, state and local governments have resulted in closures of offices and factories and disrupted supply chains. The pandemic also has taxed healthcare systems both in the U.S. and around the world, resulting in disruption to or temporary suspension of clinical trials. The nature, extent and duration of the COVID-19 pandemic remains uncertain and the time needed for businesses and healthcare systems to recover remains unknown. The full impact of the pandemic on the economy, including the capital markets, also remains unknown. The continuation of prolonged adverse economic conditions (including due to any resurgence or second wave of COVID-19 infections) could limit the Company's access to financial resources from the capital markets and other sources. It is not possible to predict the full impact of the COVID-19 pandemic on the Company's business and access to capital in the future. Although the Company has continued to enroll patients in its SUL-DUR phase 3 registration trial, or ATTACK trial, some clinical sites in high COVID-19 impact areas have experienced disruptions in new patient enrollment due to redirection of resources as dictated by local conditions. Furthermore, from March 2020 to June 2020, GARDP, with the Company's full agreement, had temporarily paused patient enrollment into the zoliflodacin Phase 3 registration trial at U.S. sites and activation of new clinical trial sites in ex-U.S. regions.

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, or U.S. GAAP. The consolidated financial statements include the Company's accounts and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with U.S. GAAP requires management to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenue and expenses during the reporting period. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the recognition of revenue and the recognition of research and development expenses. 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.

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

Fair Value Measurements

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

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

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

Level 3 Inputs—Instruments with primarily unobservable value drivers.

The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of assets or liabilities between Level 1, Level 2 or Level 3 during the years ended December 31, 2020 and 2019.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. Cash and cash equivalents include cash held in banks, money market instruments, corporate and municipal notes, U.S. Treasury securities and federal agency securities. Cash equivalents are stated at fair value. The amount of cash equivalents included in cash and cash equivalents was approximately $49.1 million and $13.9 million as of December 31, 2020 and 2019, respectively.

Short-Term Investments

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

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

Concentrations of Credit Risk and of Significant Suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and short-term investments. 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.

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

The Company is dependent on third-party manufacturers to supply active pharmaceutical ingredient, or API, and drug product for research and development activities for its programs, including clinical trial testing. These programs could be adversely affected by a significant interruption in the supply of API or drug product.

Deferred Financing Costs

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

Property and Equipment

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

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

Impairment of Long-Lived Assets

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

Segment Information

The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions. As of December 31, 2020 and 2019, all of the Company's long-lived assets were domiciled in the United States.

Revenue Recognition

Effective January 1, 2018, the Company adopted Accounting Standards Codification, or ASC, Topic 606, *Revenue from Contracts with Customers*, or ASC 606. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, and financial instruments. Under ASC 606, the Company recognizes revenue when a customer obtains control of promised goods or services, in an amount that reflects the consideration that the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in

the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assessed the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied as services are rendered.

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

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

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

Licenses of intellectual property

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

Customer options

If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options

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

Milestone payments

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

Government Contracts and Grant Agreements

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

Research and Development Costs

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

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

Patent Costs

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

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

Stock-Based Compensation

The Company measures stock-based awards based on the estimated fair value of the award on the date of the grant and recognizes compensation expense for those awarded to employees and directors over the requisite service period, which is generally the vesting period of the respective award, and for those awarded to nonemployees over the period during which services are rendered by nonemployees until completed. Forfeitures are accounted for as they occur. The Company has historically issued stock-based awards with only service-based vesting conditions and records the expense for these awards using the straight-line method.

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

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option pricing model. The Company lacks company-specific historical and implied volatility information for its stock. The Company estimates its expected stock price volatility based on the historical volatility of publicly traded peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method. The "simplified" method estimates the expected term of stock options as the mid-point between the weighted average time to vesting and the contractual maturity. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. There is no expected dividend yield since the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future.

Income Taxes

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

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

Basic and Diluted Net Loss Per Share

Net earnings or loss per share is calculated in accordance with the applicable accounting guidance provided in ASC 260, *Earnings per Share.* The Company uses the two-class method for the computation and presentation of net income (loss) per common share. The two-class method is an earnings allocation formula that calculates basic and diluted net income (loss) per share for each class of common stock separately based on
dividends declared and participation rights in undistributed earnings as if all such earnings had been distributed during the period. Under the two-class method, warrants issued to the investors in connection with the First Private Placement and the Second Private Placement are assumed to participate in undistributed earnings on an as-exercised basis, in accordance with the respective warrant agreements. Undistributed net losses are allocated entirely to common stockholders since the participating security has no contractual obligation to share in the losses.

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

Basic net income (loss) per share is computed by dividing the net income (loss) by the weighted average number of shares of common stock outstanding for the period. Diluted net income (loss) is computed by adjusting net income (loss) to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net income (loss) per share is computed by dividing the diluted net income (loss) by the weighted average number of common shares outstanding for the period, including potential dilutive common shares assuming the dilutive effect of common stock equivalents.

Recently Adopted Accounting Pronouncements

Effective January 1, 2020, the Company adopted the requirements under the FASB ASU 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement*, which eliminates, adds and modifies certain disclosure requirements for fair value measurements. The adoption of the new guidance did not affect the Company's consolidated financial statements.

Effective January 1, 2020, the Company adopted the provisions of FASB ASU 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606.* This update clarifies the interaction between Topic 808, Collaborative Arrangements, and Topic 606, *Revenue from Contracts with Customers*. The guidance is required to be applied retrospectively to the date of initial application of Topic 606 and entities should recognize the cumulative effect of initially applying the amendments as an adjustment to the opening balance of retained earnings of the later of the earliest annual period presented and the annual period that includes the date of the entity's initial application of Topic 606. The adoption of the new guidance did not affect the Company's consolidated financial statements and did not require an adjustment to the opening balance of retained earnings.

Recently Issued Accounting Pronouncements

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*, or ASU 2019-12. The amendments in ASU 2019-12 are effective for fiscal years beginning after December 15, 2020, including interim periods therein. Early adoption of the standard is permitted. The Company does not anticipate that the adoption of ASU 2019-12 will have a material effect on the Company's consolidated financial statements.

3. Short-Term Investments

The following table summarizes the amortized cost and estimated fair value of the Company's marketable securities, which are considered to be available-for-sale investments and are included in short-term investments on the consolidated balance sheet as of December 31, 2019. The Company had no short-term investments as of December 31, 2020.

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
		(in thousands)		
Balance as of December 31, 2019:				
U.S. Treasury securities	$ 24,957	$ 5	$ —	$ 24,962
Total	$ 24,957	$ 5	$ —	$ 24,962

Certain short-term debt securities with original maturities of less than 90 days are included in cash and cash equivalents on the consolidated balance sheets and are not included in the table above. As of December 31, 2019, all investments had contractual maturities within one year.

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

4. Fair Value of Financial Instruments

The following tables set forth the Company's assets that were accounted for at fair value on a recurring basis:

	December 31, 2020			
	Fair Value Measurement Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Cash equivalents:				
Money market funds	$ 49,125	$ —	$ —	$ 49,125
Total	$ 49,125	$ —	$ —	$ 49,125

	December 31, 2019			
	Fair Value Measurement Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Cash equivalents:				
Money market funds	$ 13,949	$ —	$ —	$ 13,949
Short-term investments:				
U.S. Treasury securities	24,962	—	—	24,962
Total	$ 38,911	$ —	$ —	$ 38,911

The Company classifies its money market funds and U.S. Treasury securities as Level 1 assets under the fair value hierarchy as these assets have been valued using quoted market prices in active markets without any valuation adjustment.

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

5. Property and Equipment, net

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

	As of December 31,	
	2020	2019
Laboratory equipment	$ 1,001	$ 997
Computer software	71	71
Computer equipment	38	38
Furniture and fixtures	6	6
Total	1,116	1,112
Less: accumulated depreciation	(894)	(767)
Property and equipment, net	$ 222	$ 345

Depreciation expense was $0.1 million for each of the years ended December 31, 2020 and 2019.

6. Leases

The Company adopted ASC 842 on January 1, 2019. ASC 842 allows the Company to elect a package of practical expedients, which include: (i) an entity need not reassess whether any expired or existing contracts are or contain leases; (ii) an entity need not reassess the lease classification for any expired or existing leases; and (iii) an entity need not reassess any initial direct costs for any existing leases. Another practical expedient allows the Company to use hindsight in determining the lease term when considering lessee options to extend or terminate the lease and to purchase the underlying asset. The Company has elected to utilize this package of practical expedients and has not elected the

hindsight methodology in its implementation of ASC 842. Adoption of the standard did not result in a material cumulative effect requiring adjustment to retained earnings as of January 1, 2019.

The Company determined that it held one significant operating lease as of January 1, 2019, consisting of 20,062 square feet of office and laboratory space in Waltham, Massachusetts that expires in December 2022 pursuant to a May 2015 lease with AstraZeneca, or the AZ lease, as amended in February 2018. During each of the years ended December 31, 2020 and December 31, 2019, the Company recorded lease expense of $0.6 million related to this lease. The Company has two additional operating leases that are included in its lease accounting which are not considered significant.

In calculating the present value of future lease payments, the Company utilized its incremental borrowing rate based on the remaining lease term at the date of adoption. The AZ lease contains a renewal option that can extend the lease for three years. Because the Company is not reasonably certain to exercise this renewal option, the option is not considered in determining the lease term, and associated potential additional payments are excluded from lease payments. The Company has elected to account for each lease component and its associated non-lease components as a single lease component and has allocated all of the contract consideration across lease components only. The Company has existing net leases in which the non-lease components (e.g., common area maintenance) are paid separately from rent based on actual costs incurred and therefore are not included in the operating lease right-of-use assets and lease liabilities and are reflected as an expense in the period incurred.

The following table summarizes the presentation of the Company's operating leases in its consolidated balance sheet (in thousands):

	As of December 31, 2020	As of December 31, 2019
Assets		
Operating lease right-of-use assets	$ 1,141	$ 1,620
Liabilities		
Operating lease liabilities, current	$ 617	$ 506
Operating lease liabilities, net of current portion	704	1,321
Total operating lease liabilities	$ 1,321	$ 1,827

The operating lease right-of-use assets and operating lease liabilities balances relate primarily to amounts associated with the AZ lease. Future minimum lease payments under non-cancelable leases were as detailed below (in thousands):

Fiscal Year	As of December 31, 2020
2021	$ 717
2022	737
2023	1
Total undiscounted lease payments	1,455
Less: imputed interest	(134)
Total operating lease liabilities	$ 1,321

As of December 31, 2020, the weighted-average remaining lease term was 2.0 years and the weighted-average incremental borrowing rate used to determine the operating lease right-of-use assets was 9.1%.

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

7. Accrued Expenses and Other Current Liabilities

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

	As of December 31,	
	2020	2019
Accrued compensation and benefits	$ 2,935	$ 2,490
Accrued contract manufacturing	2,959	1,550
Accrued clinical	504	606
Accrued professional services	435	530
Accrued research	349	275
Current portion of operating lease liabilities	617	506
Other	106	295
Total accrued expenses and other current liabilities	$ 7,905	$ 6,252

8. Funding Arrangements

NIH

In June 2020, the Company entered into a contract with the National Institute of Allergy and Infectious Diseases, or NIAID, part of the National Institutes of Health, or NIH, which was effective beginning July 1, 2020 and provides the Company with reimbursement of certain qualified expenses incurred. The initial award consists of approximately $3.0 million, with the potential to increase up to $15.5 million, and will be used to develop novel molecules from the Company's non-β-lactam inhibitor, or NBP, platform. Funding from the contract will support research towards developing molecules with expanded Gram-negative spectrum against antibiotic resistant bacterial pathogens including *E. coli*, *Acinetobacter*, *Pseudomonas* and *Klebsiella*. The contract will be accounted for consistent with the Company's Government Contracts and Grant Agreements accounting policy.

The Company recognized grant income in connection with the NIH contract of $1.3 million during the year ended December 31, 2020. The Company received payments of $0.6 million under this contract during the year ended December 31, 2020. As of December 31, 2020, the Company's receivables for unreimbursed, eligible costs incurred under the NIH contract totaled $0.7 million.

CARB-X

In March 2017 and October 2017, the Company entered into funding arrangements with the Trustees of Boston University to utilize funds from the U.S. government through the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, program, in support of the ETX0282CPDP and ETX0462 programs. In June 2020 CARB-X exercised an option that resulted in an increase in the amount of specified research expenditures of the Company that could be covered from $16.8 million to $18.2 million from April 2017 through September 2021. Through December 31, 2020, the Company has received $9.5 million in payments and recorded $10.3 million of grant income under these funding arrangements.

The Company recognized grant income in connection with the CARB-X agreements of $2.3 million for each of the years ended December 31, 2020 and 2019. The Company received $2.4 million and $2.6 million of payments under the grants during the years ended December 31, 2020 and 2019, respectively. The Company recorded a receivable to reflect unreimbursed, eligible costs incurred under the CARB-X agreements in the amount of $1.1 million and $1.2 million as of December 31, 2020 and December 31, 2019, respectively.

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

9. License and Collaboration Agreements

GARDP

In July 2017, the Company entered into a collaboration agreement with the Global Antibiotic Research and Development Partnership, or GARDP, for the development and commercialization of a product candidate containing zoliflodacin in certain countries. Under the terms of the collaboration agreement, GARDP will use commercially reasonable endeavors to perform and fully fund the Phase 3 registration trial, including the manufacture and supply of the product candidate containing zoliflodacin, in uncomplicated gonorrhea. The Company is obligated to commit reasonably sufficient time and resources to collaborate in the design of the Phase 3 registration 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. The Phase 3 registration trial was initiated in September 2019 with activation of U.S. sites. In March 2020, in response to the COVID-19 pandemic, GARDP, with the Company's full agreement, had temporarily paused patient enrollment at U.S. sites and activation of new clinical trial sites in ex-U.S. regions. In July 2020, GARDP resumed patient enrollment into the Phase 3 registration trial at U.S. sites and activated a new clinical trial site in the Netherlands.

In addition, under the collaboration agreement, the Company has granted GARDP a worldwide, fully paid, exclusive and royalty-free license, with the right to sublicense, to use its zoliflodacin technology in connection with GARDP's development, manufacture and commercialization of zoliflodacin in low-income and specified middle-income countries. The Company has retained commercial rights in all other countries worldwide, including the major markets in North America, Europe and Asia-Pacific. The Company has also retained the right to use and grant licenses to its zoliflodacin technology to perform its obligations under the collaboration agreement and for any purpose other than gonorrhea or community-acquired indications. If the Company believes that the results of the Phase 3 registration trial of zoliflodacin would be supportive of an application for marketing approval, it is obligated to use its 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.

Zai Lab

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

The Company received an upfront, non-refundable payment of $5.0 million, milestone payments of $7.0 million, research support funding of $0.6 million and certain other reimbursable registration trial costs of $4.2 million, less applicable taxes of $2.1 million, from Zai Lab through December 31, 2020. During the year ended December 31, 2020, the Company recognized no revenue under the Zai Agreement, and during the year ended December 31, 2019, the Company recognized $7.0 million of revenue under the Zai Agreement. The Company is eligible to receive up to an aggregate of $91.0 million in additional research and development support payments and

development, regulatory and sales milestone payments related to SUL-DUR, imipenem and other combinations with the licensed products. In the event the Chinese regulatory agency, National Medical Products Administration, requires a modification or supplement to the trial protocol, and the Company delays Zai Lab from proceeding with such modified protocol and subsequently obtaining regulatory approval for the pivotal study of SUL-DUR in China, then the future sales-based milestone payments that become due to the Company will be reduced by an agreed upon amount that increases with the length of the delay. Zai Lab will pay the Company a tiered royalty equal to a high-single digit to low-double digit percentage based on annual net sales of licensed products in the territory, subject to specified reductions for the market entry of competing products, loss of patent coverage of licensed products and for payments owed to third parties for additional rights necessary to commercialize licensed products in the territory.

The Company determined the $5.0 million non-refundable upfront payment was the entire transaction price at the outset of the Zai Agreement. All other future potential milestone payments were excluded from the transaction price as they were fully constrained as the risk of significant reversal of revenue had not yet been resolved. At the outset of the Zai Agreement, the achievement of the future potential milestones was not within the Company's control and was subject to certain research and development success, regulatory approvals or commercial success and therefore carried significant uncertainty. The Company reevaluates the likelihood of achieving the future milestones at the end of each reporting period. Future development milestone revenue from the arrangement will be recognized as revenue in the period when it is no longer probable that revenue attributable to the milestone will result in a significant reversal of cumulative revenue. Payments received for research support and reimbursable clinical trial costs are recorded as an offset to research and development expense during the period in which the qualifying expenses are incurred.

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

10. Stockholders' Equity

Common Stock

Each holder of common stock shall be entitled to one vote for each share of common stock held of record by such holder on all matters on which stockholders generally are entitled to vote. Common stockholders are entitled to receive dividends when and if declared by the board of directors, out of any funds legally available. As of December 31, 2020, no dividends have been declared or paid.

Second Private Placement

On August 27, 2020, the Company entered into the Second Securities Purchase Agreement with the Investors, including existing stockholder Innoviva, pursuant to which the Company issued and sold to the Investors in a private placement (i) 8,183,878 newly issued shares of common stock of the Company at $2.675 per share, (ii) warrants to purchase an aggregate of 9,345,794 shares of common stock with and exercise price of $2.675, and (iii) pre-funded warrants, in lieu of common stock, to purchase an aggregate of 1,161,916 shares of common stock, with an exercise price of $0.001 per share, resulting in aggregate gross proceeds of approximately $25.0 million. The closing of the Second Private Placement occurred on September 1, 2020.

The exercise price and the number of shares of common stock issuable upon exercise of each warrant is subject to appropriate adjustments in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting the Company's common stock. Each warrant is exercisable from the date of issuance and has a term of five years.

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

Registration Rights Agreement

On September 1, 2020, in connection with the Second Securities Purchase Agreement, the Company entered into a registration rights agreement, or the Second Registration Rights Agreement, with the Investors. Pursuant to the Second Registration Rights Agreement, the Company agreed to prepare and file a registration statement with the SEC, within 45 days after the closing of the Second Private Placement for purposes of registering the resale of the shares of common stock, shares of common stock issuable upon exercise of the warrants, the warrants and any shares of common stock issued as a dividend or other distribution with respect to the shares or shares of common stock issuable upon exercise of the warrants. The registration statement was filed with the SEC on October 5, 2020, and declared effective by the SEC on October 13, 2020.

First Private Placement

On April 12, 2020, the Company entered into the First Securities Purchase Agreement, with Innoviva, pursuant to which the Company issued and sold to Innoviva 14,000,000 newly issued shares of common stock of the Company at $2.50 per share, and warrants to purchase up to 14,000,000 shares of common stock with an exercise price per share of $2.50.

Under the First Securities Purchase Agreement, the First Private Placement occurred in two tranches. At the closing of the first tranche, which occurred on April 22, 2020, or the First Closing, Innoviva purchased 1,322,510 shares of common stock and warrants to purchase 1,322,510 shares of common stock, for an aggregate gross purchase price of approximately $3.3 million. At the closing of the second tranche, which occurred on June 11, 2020, or the Second Closing, Innoviva purchased the remaining 12,677,490 shares of common stock and warrants to purchase 12,677,490 shares of the common stock for an aggregate gross purchase price of approximately $31.7 million.

As of December 31, 2020, Innoviva owned approximately 51.0% of the Company’s outstanding common stock.

Investor Rights Agreement

At the First Closing, Innoviva and the Company entered into an investor rights agreement, or the Investor Rights Agreement, which provides that for so long as Innoviva and its affiliates hold at least 15% of the outstanding shares of the Company’s common stock on a fully-diluted basis, Innoviva shall have the right to designate two directors to the board of directors of the Company, or the Board; and for so long as Innoviva and its affiliates hold at least 8% of the outstanding shares of the Company’s common stock on a fully-diluted basis, Innoviva shall have the right to designate one director to the Board, subject to certain qualifications and conditions in the Investor Rights Agreement. The Investor Rights Agreement also provides for participation rights for Innoviva to participate pro rata in future offerings of securities by the Company.

Registration Rights Agreements

At the First Closing, the Company and Innoviva entered into a registration rights agreement, or the First Registration Rights Agreement, pursuant to which, among other things, the Company agreed to prepare and file with the SEC a registration statement with respect to resales of the shares of common stock and the warrants purchased by Innoviva under the First Securities Purchase Agreement within 30 days of the First Closing. Innoviva and the Company subsequently signed a waiver to this agreement allowing the Company to file a registration statement with the SEC no later than August 31, 2020. The registration statement was filed with the SEC on August 6, 2020, and declared effective by the SEC on August 14, 2020.

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

Warrants

As of December 31, 2020, outstanding warrants to purchase shares of the Company's common stock are as follows:

Shares Underlying Outstanding Warrants	Exercise Price	Expiration Date
1,322,510	$ 2.50	April 22, 2025
12,677,490	$ 2.50	June 11, 2025
9,345,794	$ 2.675	September 1, 2025
23,345,794		

Aspire Common Stock Purchase Agreement

In October 2019, the Company entered into a common stock purchase agreement, or CSPA, with Aspire Capital Fund, LLC, or Aspire, which provided that, upon the terms and subject to the conditions and limitations set forth therein, Aspire is committed to purchase up to an aggregate of $20.0 million of shares of the Company's common stock over the 30-month term of the CSPA. Under the CSPA, on any trading day selected by the Company on which the closing price of its common stock is equal to or greater than $0.25 per share, the Company has the right, in its sole discretion, to present Aspire with a purchase notice directing Aspire to purchase up to 50,000 shares of common stock per business day, at a purchase price equal to the lesser of the lowest sale price of common stock on the purchase date, or the arithmetic average of the three lowest closing sale prices during the 10 consecutive business days ending on the trading day immediately preceding the purchase date. The Company and Aspire also may mutually agree to increase the number of shares that may be sold to as much as 2,000,000 shares per business day.

In addition, on any date on which the Company submits a purchase notice to Aspire in an amount equal to 50,000 shares, the Company also has the right, in its sole discretion, to present Aspire with a volume-weighted average price purchase notice, or the VWAP Purchase Notice, directing Aspire to purchase an amount of stock equal to up to 30% of the aggregate shares of the Company's common stock traded on its principal market on the next trading day, or the VWAP Purchase Date, subject to a maximum number of shares the Company may determine. The purchase price per share pursuant to such VWAP Purchase Notice is generally 97% of the volume-weighted average price for the Company's common stock traded on its principal market on the VWAP Purchase Date.

The Company controls the timing and amount of any sales to Aspire, and is not limited with respect to use of proceeds or by any financial or business covenants, restrictions on future financings, rights of first refusal, participation rights, penalties or liquidated damages in the CSPA. The CSPA may be terminated by the Company at any time, at its discretion, without any cost to the Company. Aspire has no trading volume requirements or restrictions, and has no right to require any sales by the Company but is obligated to make purchases as directed by the Company in accordance with the CSPA. Aspire has agreed that neither it nor any of its agents, representatives and affiliates shall engage in any direct or indirect short-selling or hedging of common stock during any time prior to the termination of the CSPA.

As consideration for Aspire's obligation under the CSPA, the Company issued 104,167 shares of common stock to Aspire as a commitment fee, or the Commitment Shares. This $0.6 million commitment fee and $0.1 million in other transaction costs were deferred and will be charged against the gross proceeds received upon exercise by the Company as costs of equity financing within additional paid-in capital.

The CSPA further provides that the number of shares that may be sold pursuant to the CSPA will be limited to 2,626,165 shares, including the Commitment Shares, which represents 19.99% of the Company's outstanding shares of common stock as of October 21, 2019, unless stockholder approval is obtained to issue more than 19.99%. This limitation will not apply under certain circumstances specified in the CSPA. During the year ended December 31, 2020, no shares had been purchased by Aspire pursuant to the CSPA. During the year ended December 31, 2019, 50,000 shares had been purchased by Aspire pursuant to the CSPA resulting in gross proceeds of $0.3 million.

Concurrently with entering into the CSPA, the Company also entered into a registration rights agreement with Aspire, pursuant to which the Company filed with the SEC a prospectus supplement to the Company's effective shelf registration statement on Form S-3 (File No. 333-234041), registering all of the shares of common stock that may be offered to Aspire from time to time under the CSPA, including the Commitment Shares.

11. Stock-Based Compensation Expense

Stock Incentive Plan

In September 2018, the Company's board of directors adopted and its stockholders approved the 2018 Equity Incentive Plan, or the 2018 Plan, which became effective on September 25, 2018, at which point no further grants will be made under the 2015 Stock Inventive Plan, or the 2015 Plan, previously in effect. Under the 2018 Plan, the Company may grant incentive stock options, or ISOs, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. As of December 31, 2020, options to purchase an aggregate of 3,720,509 shares had been granted, restricted stock units, or RSUs, of 395,100 had been awarded, and 359,416 shares were available for future issuance under the 2018 Plan. The options issued under the 2018 Plan expire after 10 years from the date of grant.

At its inception, the aggregate number of shares of the Company's common stock available for issuance under the 2018 Plan was 2,350,000. The number of shares of the Company's common stock reserved for issuance under the 2018 Plan will automatically increase on January 1 of each year, for a period of 10 years, from January 1, 2019 continuing through January 1, 2028, by 4% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by the Company's board of directors. Accordingly, on January 1, 2021 and 2020, 1,465,494 and 531,662 shares were added to the number of available shares, respectively. The maximum number of shares that may be issued pursuant to the exercise of ISOs under the 2018 Plan is 7,500,000.

The maximum number of shares of the Company's common stock subject to awards granted under the 2018 Plan or otherwise during a single calendar year to any nonemployee directors, taken together with any cash fees paid by the Company to such nonemployee directors during the calendar year for serving on the Company's board of directors, will not exceed $500,000 in total value, or, with respect to the calendar year in which a nonemployee director is first appointed or elected to the Company's board of directors, $800,000.

All options and awards granted under the 2015 Plan consisted of the Company's common stock. As of September 25, 2018, no additional stock awards have been or will be granted under the 2015 Plan. Although the 2015 Plan was terminated as to future awards in September 2018, it continues to govern the terms of options that remain outstanding under the 2015 Plan.

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

Stock Option Activity

Stock option activity under both plans for year ended December 31, 2020 is summarized as follows:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2019	2,388,400	$ 6.20	8.44	$ 906
Granted	1,107,300	4.30		
Exercised	—	—		
Forfeited	(382,996)	5.80		
Outstanding as of December 31, 2020	3,112,704	$ 5.58	7.76	$ 44
Exercisable as of December 31, 2020	1,439,434	$ 5.81	7.02	$ —

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the options and the fair value of the Company's common stock for those options that had exercise prices lower than the fair value of the Company's common stock.

During the years ended December 31, 2020 and 2019 the weighted-average grant-date fair value per granted option was $2.95 and $3.99, respectively.

Restricted Stock Unit Activity

Restricted stock unit activity for the year ended December 31, 2020 is summarized as follows:

	Number of Units	Weighted-Average Grant Date Fair Value
Outstanding as of December 31, 2019	—	$ —
Granted	395,100	1.65
Released	—	—
Forfeited	—	—
Outstanding as of December 31, 2020	395,100	$ 1.65

Employee Stock Purchase Plan

In September 2018, the Company's board of directors and its stockholders approved the 2018 Employee Stock Purchase Plan, or the ESPP, which became effective as of September 25, 2018. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the U.S. Internal Revenue Code of 1986, as amended. The number of shares of common stock initially reserved for issuance under the ESPP was 140,000 shares. The ESPP provides for an annual increase on the first day of each year beginning in 2019 and ending in 2028, in each case subject to the approval of the board of directors, equal to the lesser of (i) 1% of the shares of common stock outstanding on the last day of the prior fiscal year or (ii) 250,000 shares; provided, that prior to the date of any such increase, the board of directors may determine that such increase will be less than the amount set forth in clauses (i) and (ii). Pursuant to the terms of the 2018 Employee Stock Purchase Plan, an additional 250,000 and 132,915 shares were added to the number of available shares effective January 1, 2021 and 2020, respectively. As of December 31, 2020, no shares of common stock had been issued under the ESPP and 404,163 shares remained available for future issuance under the ESPP. No offering period under the ESPP has been set by the Company's board of directors.

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

Stock-Based Compensation

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

	Year Ended December 31,	
	2020	2019
Research and development	$ 1,397	$ 891
General and administrative	1,554	1,530
Total stock-based compensation expense	$ 2,951	$ 2,421

The following table summarizes stock-based compensation expense by type of award (in thousands):

	Year Ended December 31,	
	2020	2019
Stock options	$ 2,898	$ 2,421
Restricted stock units	53	—
Total stock-based compensation expense	$ 2,951	$ 2,421

The following table summarizes unrecognized stock-based compensation expense as of December 31, 2020, by type of awards, and the weighted-average period over which that expense is expected to be recognized. The total unrecognized stock-based compensation expense will be adjusted for actual forfeitures as they occur.

	As of December 31, 2020	
	Unrecognized Expense (in thousands)	Weighted-average Recognition Period (in years)
Stock options	$ 5,324	2.44
Restricted stock units	$ 599	1.84

The following weighted average assumptions were used to calculate the fair value of each stock option award under the Black-Scholes option pricing model:

	Year Ended December 31,	
	2020	2019
Expected stock price volatility	82.0 %	77.8 %
Risk-free interest rate	0.5 %	2.3 %
Expected annual dividend yield	—	—
Expected life of options	6.3 years	6.1 years

12. Income Taxes

During the years ended December 31, 2020 and 2019, the Company recorded no income tax benefits for the net operating losses incurred due to its uncertainty of realizing a benefit from those items. The Company's losses before income taxes were generated in the United States and the United Kingdom.

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

Net loss before the provision for income taxes for the years ended December 31, 2020 and 2019, consisted of the following (in thousands):

	Year Ended December 31,	
	2020	2019
United Kingdom	$ 38,280	$ 32,725
United States	12,216	10,448
	$ 50,496	$ 43,173

There was no provision for income taxes for the year ended December 31, 2020. The provision for income taxes for the year ended December 31, 2019 consisted of the following (in thousands):

	Year Ended December 31, 2019
Current	
Federal	$ —
State	17
Foreign	660
Total current	677
Deferred	
Federal	—
State	—
Foreign	—
Total deferred	—
Total income taxes	$ 677

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

	Year Ended December 31,	
	2020	2019
Income tax benefit computed at U.S. statutory tax rate	21.0 %	21.0 %
State taxes, net of federal benefit	6.6	6.9
Foreign rate differential	(1.5)	(3.0)
Disregarded entity	15.9	15.9
Research and development tax credits	1.4	1.4
Permanent difference	(0.6)	0.1
Valuation allowances	(45.7)	(42.4)
Rate change	3.6	—
Other	(0.7)	—
Foreign withholding tax	—	(1.5)
Effective income tax rate	(0.0)%	(1.6)%

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

Net deferred tax assets consisted of the following (in thousands):

	As of December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 57,265	$ 36,151
Tax credit carryforwards	4,345	3,507
Accrued expenses and other	3,099	2,037
Total deferred tax assets	64,709	41,695
Deferred tax liabilities:		
ASC 842 right-of-use asset	(312)	(442)
Total deferred tax liabilities	(312)	(442)
Valuation allowance	(64,397)	(41,253)
Net deferred tax assets	$ —	$ —

Net operating losses generated in years ending after December 31, 2018 will be carried forward indefinitely and can no longer be carried back, and net operating losses generated in years beginning after December 31, 2017, can only reduce taxable income by 80% when utilized in a future period. As of December 31, 2020, the Company had federal and state net operating loss carryforwards, or NOLs, of $119.8 million and $121.2 million, respectively, which begin to expire in 2035. Included in the $119.8 million of federal net operating losses are losses of $107.1 million that will carry forward indefinitely as a result of the Tax Cuts and Jobs Act. As of December 31, 2020, the Company had federal and state research and development tax credits carryforwards of $3.4 million and $1.2 million, respectively, which begin to expire in 2035 and 2026, respectively.

Utilization of the 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 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 stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. During 2020, Innoviva purchased over 50% of the Company's common stock. This ownership change may result in a limitation of the Company's NOLs. The Company has not conducted a study to assess whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. Ownership changes may limit the amount of NOLs and tax credit carryforwards that could be utilized annually to offset future taxable income. The amount of the annual limitation is determined based on the Company's value immediately prior to the ownership change. Subsequent significant changes in ownership could affect the limitations in future years. Any limitation may result in expiration of a portion of the net operating loss carryforwards or tax credit carryforwards before utilization.

As of December 31, 2020, the Company had NOLs in the United Kingdom of $128.7 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 the federal, state and foreign deferred tax assets. Accordingly, a full valuation allowance of $64.4 million has been established against the deferred tax assets as of December 31, 2020. Management reevaluates the positive and negative evidence at each reporting period.

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

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2020 and 2019 related primarily to the increases in NOLs and research and development tax credit carryforwards and were as follows (in thousands):

	Year Ended December 31,	
	2020	2019
Valuation allowance at beginning of year	$ (41,253)	$ (23,459)
Increases recorded to income tax provision	(23,144)	(17,794)
Valuation allowance at end of year	$ (64,397)	$ (41,253)

The Company has not recorded an amount for unrecognized tax benefits or related interest and penalties accrued as of December 31, 2020. The Company files income tax returns in the United States, Massachusetts and the United Kingdom. The federal and state returns are generally subject to tax examinations for the tax years ended December 31, 2015 to the present. The statute of limitations for assessment by the United Kingdom is open for the tax years since 2015. There are currently no pending tax examinations. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service and state tax authorities to the extent utilized in a future or prior period. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision.

13. Net Loss per Share

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

	Year Ended December 31,	
	2020	2019
Numerator:		
Net loss	$ (50,496)	$ (43,850)
Net loss attributable to common stockholders—basic and diluted	$ (50,496)	$ (43,850)
Denominator:		
Weighted average common stock outstanding—basic and diluted	24,060,615	13,160,357
Net loss per share attributable to common stockholders—basic and diluted	$ (2.10)	$ (3.33)

The following outstanding securities have been excluded from the computation of diluted weighted average shares outstanding for the year ended December 31, 2020 and 2019, respectively, as they would have been anti-dilutive:

	As of December 31,	
	2020	2019
Options to purchase shares of common stock	3,112,704	2,388,400
Warrants to purchase shares of common stock	23,345,794	—
Unvested restricted stock units	395,100	—
	26,853,598	2,388,400

14. Commitments

Lease Commitments

The Company has an operating lease agreement for its office and laboratory space with AstraZeneca. See Note 6, *Leases*, for additional information.

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

AstraZeneca Subscription Agreement

In connection with the Company's spin-out from AstraZeneca in 2015, the Company entered into a business transfer and subscription agreement with AstraZeneca, or the AstraZeneca Subscription Agreement, pursuant to which the Company agreed to pay AstraZeneca a one-time milestone payment of $5.0 million within three months of achieving a specified cumulative net sales milestone for durlobactam. This milestone payment will be automatically waived should the Company's common stock trade on Nasdaq at or above a specified price at the time it achieves such specified cumulative net sales milestone for durlobactam. The Company is also obligated to pay AstraZeneca a one-time milestone payment of $10.0 million within two years of achieving the first commercial sale of zoliflodacin. At the Company's election, either milestone payment may be paid in cash, common stock, or a combination of cash and common stock. Additionally, the Company is obligated to pay AstraZeneca tiered, single-digit, per-country royalties on the annual worldwide net sales of durlobactam and zoliflodacin.

15. Related Party Transactions

AstraZeneca

The Company was formed in May 2015 as a wholly owned subsidiary of AstraZeneca. Prior to the closing of the initial public offering on September 28, 2018, AstraZeneca was the sole holder of Series A preferred stock. Upon the closing of the initial public offering, all shares of preferred stock converted into shares of common stock. AstraZeneca continues to maintain an ownership interest in the Company. The Company has an operating lease agreement for its office and laboratory space with AstraZeneca. See Note 6, *Leases*, for additional information.

Pharmaron Beijing Co., Ltd. (China)

The Company contracts with Pharmaron Beijing Co., Ltd. (China), or Pharmaron, to provide various medicinal chemistry research, manufacturing development and clinical services related to the Company's ongoing product candidates. The Company began utilizing Pharmaron as a service provider prior to the spin-out in 2015, and this relationship has continued through 2020. In 2019, the Senior Vice President of Strategic Partnerships at Pharmaron began sharing a household with the Company's Chief Executive Officer and, as a result, the Company considers the agreements between the Company and Pharmaron to be related-party transactions. The Company recorded expense of $5.0 million and $7.2 million during the years ended December 31, 2020 and December 31, 2019, respectively, for services pursuant to multiple Pharmaron agreements. Amounts due to Pharmaron were $2.0 million and $0.8 million as of December 31, 2020 and December 31, 2019, respectively.

16. Benefit Plans

The Company has a tax-qualified employee savings and retirement 401(k) plan, covering all qualified employees. Participants may elect a salary deferral up to the statutorily prescribed annual limit for tax-deferred contributions. The Company made matching contributions of $0.3 million and $0.2 million for the years ended December 31, 2020 and 2019, respectively.

Exhibit 21.1

SUBSIDIARIES OF ENTASIS THERAPEUTICS HOLDINGS INC.

Name	Jurisdiction of Incorporation
Entasis Therapeutics Inc.	Delaware
Entasis Therapeutics Limited	United Kingdom
Entasis Therapeutics Security Corporation	Massachusetts
Entasis Therapeutics (Ireland) Limited	Ireland

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

The Board of Directors
Entasis Therapeutics Holdings Inc.:

We consent to the incorporation by reference in the registration statements (No. 333-228384, 333-230593, 333-238076 and 333-2411672) on Form S-8 and (No. 333-234041, 333-241683 and 333-249315) on Form S-3 of Entasis Therapeutics Holdings Inc. of our report dated March 23, 2021, with respect to the consolidated balance sheets of Entasis Therapeutics Holdings Inc. and subsidiaries as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for the years then ended, and the related notes, which report appears in the December 31, 2020 annual report on Form 10-K of Entasis Therapeutics Holdings Inc.

/s/ KPMG LLP

Boston, Massachusetts
March 23, 2021

Exhibit 31.1

CERTIFICATION PURSUANT TO RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Manoussos Perros, certify that:

1. I have reviewed this Annual Report on Form 10-K of Entasis Therapeutics Holdings Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 23, 2021

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

Exhibit 31.2

CERTIFICATION PURSUANT TO RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Michael Gutch, certify that:

1. I have reviewed this Annual Report on Form 10-K of Entasis Therapeutics Holdings Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 23, 2021

By: /s/ Michael Gutch, Ph.D.
Michael Gutch, Ph.D.
Chief Financial Officer and Chief Business Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Entasis Therapeutics Holdings Inc. (the "Company") for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his or her knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 23, 2021

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

Date: March 23, 2021

By: /s/ Michael Gutch, Ph.D.
Michael Gutch, Ph.D.
Chief Financial Officer and Chief Business Officer
(Principal Financial and Accounting Officer)