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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2019

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 For the transition period from ____to____**

Commission file number 001-38266

SPERO THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**46-4590683**
State or other jurisdiction of incorporation or organization	**(I.R.S. Employer Identification No.)**
675 Massachusetts Avenue, 14th Floor Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code (857) 242-1600

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, $0.001 par value per share	SPRO	The Nasdaq Global Select 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 Act. Yes ☐ No ☒

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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.

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

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

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

The aggregate market value of Common Stock held by non-affiliates of the registrant computed by reference to the price of the registrant's Common Stock as of June 28, 2019, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $150.5 million (based on the last reported sale price on the Nasdaq Global Market as of such date). As of March 9, 2020, there were 20,328,340 shares of the registrant's Common Stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

None.

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PART I

Forward-Looking Information

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue” or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, design, progress and results of, including interim data from, our preclinical studies and clinical trials, and our research and development programs;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the timing or likelihood of regulatory filings and approvals;
- the commercialization of our product candidates, if approved;
- the pricing, coverage and reimbursement of our product candidates, if approved;
- the implementation of our business model and strategic plans for our business and product candidates and our Potentiator Platform;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and our Potentiator Platform;
- our ability to enter into strategic arrangements and/or collaborations and the potential benefits of such arrangements;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- our ability to continue as a going concern;
- our financial performance;
- developments relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under Part I, Item 1A. “Risk Factors”.

Any forward-looking statements in this Annual Report on Form 10-K reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Part I Item 1A. “Risk Factors” and elsewhere in this Annual Report on Form 10-K. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. 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.

Item 1. Business.

Overview

We are a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing and commercializing treatments in high unmet need areas involving multi-drug resistant, or MDR, bacterial infections and rare diseases. Our most advanced product candidate, Tebipenem Pivoxil Hydrobromide, or tebipenem HBr (previously SPR994), is designed to be the first oral carbapenem-class antibiotic for use in adults to treat MDR Gram-negative infections. Treatment with effective orally administrable antibiotics may prevent hospitalizations for serious infections and enable earlier, more convenient and cost-effective treatment of patients after hospitalization. We are also developing SPR720, a novel oral antibiotic designed for the treatment of a rare, orphan disease caused by pulmonary non-tuberculous mycobacterial infections, or NTM disease. In addition, we have a platform technology known as our Potentiator Platform, that includes an IV-administered product candidate, SPR206, being developed to treat MDR Gram-negative infections in the hospital. We believe that our novel product candidates, if successfully developed and approved, would have a meaningful patient impact and significant commercial applications for the treatment of MDR infections in both the community and hospital settings.

Antibiotic-resistant bacteria are one of the largest threats to global health, and their prevalence is increasing. While the majority of life-threatening infections historically resulting from antibiotic-resistant bacteria are acquired in the hospital setting, there is an increasing incidence of MDR pathogens in the community setting. Antibiotics used currently for first-line empiric treatment of MDR bacterial infections suffer from significant limitations and risks, including narrow spectrums of coverage and safety and tolerability concerns, and they can be associated with serious adverse effects. In addition, there are no oral antibiotics commercially available that can reliably be used in adults with MDR Gram-negative bacterial infections. This limits the ability of physicians to prevent hospitalizations and transition patients to their home from the hospital after receiving IV-administered therapy. The increasing prevalence of drug resistance and MDR Gram-negative bacteria, as well as the limitations of existing therapies and traditional drug development approaches, highlight the critical need for novel therapies, and in particular orally administrable agents, that are capable of overcoming these obstacles to effective patient treatment.

To address the foregoing, we are developing a portfolio of novel product candidates, including:

- **Oral tebipenem HBr: Novel Antibiotic with Potential to be the First Oral Carbapenem for Use in Adults.** tebipenem HBr (tebipenem pivoxil hydrobromide), is our novel oral formulation of tebipenem, a carbapenem-class antibiotic marketed by Meiji Seika Pharma Co. Ltd., or Meiji, in Japan as Orapenem since 2009 for common pediatric infections. Carbapenems are an important class of antibiotics because they are safe and effective against drug-resistant Gram-negative bacterial infections. Carbapenem use has increased dramatically as a result of the rising resistance to commonly used agents such as fluoroquinolones and cephalosporin antibiotics. Carbapenems are now considered as the standard-of-care for treating these resistant bacteria, but they are currently only available intravenously for such indications. Following the FDA's acceptance of our investigational new drug, or IND, application for tebipenem HBr treatment of complicated urinary tract infections, or cUTI, we initiated the single pivotal Phase 3 clinical trial, which is entitled ADAPT-PO, that is required for approval of tebipenem HBr to treat cUTI, and which continues to enroll patients. The ADAPT-PO trial is designed as a double-blind, double-dummy trial to compare oral tebipenem HBr with an existing standard of care intravenous, or IV, antibiotic, ertapenem, in approximately 1,200 patients with cUTI or acute pyelonephritis, randomized 1:1 in each arm. In October 2019, an independent review committee issued a positive recommendation to continue the trial using the protocol-defined dose without modification following its analysis of interim pharmacokinetic data from the first 33 patients dosed with tebipenem HBr in the trial. The trial is enrolling well and we expect to report top-line data from the Phase 3 clinical trial in the third quarter of 2020. In March 2019, the FDA granted Fast Track Designation for tebipenem HBr for the treatment of cUTI and acute pyelonephritis, a designation that provides opportunities for more frequent interaction with the FDA review team to expedite development and review as well as the potential for rolling review of the NDA upon request and agreement with the FDA. In addition to cUTI, we believe that tebipenem HBr has the potential to treat other serious and life-threatening infections, including community acquired bacterial pneumonia, or CABP, for which we could receive funding support from the Biomedical Advanced Research and Development Authority, or BARDA, subject to BARDA exercising its future option under our BARDA award, as further described in this section.

Prior Safety and Efficacy Experience with Tebipenem Pivoxil in Japan

Our clinical strategy is supported by extensive safety data underlying tebipenem pivoxil's regulatory approval in Japan and long-standing use in Japan for common pediatric infections. Approximately 1,200 subjects, including approximately 741 adults, have been dosed with tebipenem pivoxil at a range of doses in clinical and pharmacologic studies. In addition, Meiji has completed a post-market study including 3,540 patients following the safety and tolerability of tebipenem pivoxil at the approved dose. In addition, two exploratory Phase 2 trials were conducted in Japan in patients with cUTI, the first indication in which we intend to study tebipenem HBr. We have the rights to all data from the registration and post-marketing studies conducted by Meiji.

In addition, we received Qualified Infectious Disease Product, or QIDP, designation from the FDA for tebipenem HBr for the treatment of cUTI, CABP, and moderate to severe diabetic foot infections, or DFI. The QIDP designation was created by the Generating Antibiotic Incentives Now, or GAIN, Act and creates incentives for the development of certain antibiotics that treat serious or life-threatening infections. QIDP designation entitles us to priority review of tebipenem HBr for regulatory approval by the FDA. The QIDP designation for tebipenem HBr, however, does not guarantee a faster development process or ensure FDA approval.

We have global commercialization rights to tebipenem HBr, except in certain contractually specified Asian countries which are licensed to Meiji. We believe that our intellectual property portfolio will provide us global protection for tebipenem HBr, including in the United States and Europe, through 2038.

- ***Oral SPR720: Novel Oral Antibiotic Designed for Treatment of Pulmonary Non-tuberculous Mycobacterial Disease.*** SPR720 is our novel orally available product candidate designed for the treatment for NTM disease, a rare orphan disease. Lung infections caused by NTM disease are rare, and occur most frequently in patients with compromised immune systems or abnormal pulmonary anatomy. Such conditions include human immunodeficiency virus, or HIV, or respiratory conditions, such as cystic fibrosis, chronic obstructive pulmonary disease, asthma and bronchiectasis. The annual prevalence of NTM disease is increasing at an estimated rate of 8% per year. The current treatment for pulmonary NTM disease is at least twelve months and involves combination therapy, often including three or more antibiotics, including some, such as aminoglycosides, that are parenterally administered. There are currently no oral treatments specifically approved for use to treat NTM disease. Treatment failure is common and is often due to lack of clearance of bacteria, no impact on patients' quality of life, poor compliance or patients' inability to tolerate the regimen. Many patients experience progressive lung disease and mortality is high. We believe SPR720, if successfully developed, has the potential to be the first oral antibiotic specifically approved for the treatment of this debilitating rare disease. *In vitro* and *in vivo* studies have demonstrated the potency of SPR720 against a range of bacteria causing NTM infection, including both *Mycobacterium avium* complex and *Mycobacterium abscessus*, a highly resistant strain causing infections with high mortality.

  We initiated a Phase 1 clinical trial of SPR720 in January 2019, designed as a double-blind, placebo-controlled, single and multiple ascending dose, multi-cohort study in healthy subjects, and reported preliminary findings from the trial in December 2019. Analysis of the blinded data from this trial supports further development of the compound as an oral agent for the treatment of NTM disease. Specifically, there were no serious adverse events reported and all participants completed the trial. Although the data remain blinded, an analysis of preliminary data indicates that SPR720 was generally well-tolerated at doses up to 1000 mg over the maximum studied duration of 14 days. Preliminary analyses of pharmacokinetic, or PK, data across the cohorts show no significant impact of either advanced age or administration with food on PK variables. At doses of 500 mg or higher, the mean plasma drug exposures of SPR719, the active metabolite of SPR720, are consistent with those suggested by *in vitro* and *in vivo* models of SPR720 to be necessary for clinical efficacy against target NTM pathogens.

  We plan to meet with the FDA in the first half of 2020, submit an IND to the FDA in the second half of 2020 and, subject to FDA acceptance of the IND, initiate a Phase 2a clinical trial evaluating SPR720 in patients with NTM pulmonary disease due to *Mycobacterium avium* complex in the second half of 2020. In March 2020, the FDA granted orphan drug designation for SPR720, a designation that is given to drugs intended to treat a rare disease or condition that affects fewer than 200,000 persons in the United States. An orphan drug designation can provide specific benefits including up to seven years of market exclusivity in the United States upon regulatory approval. In February 2019, we received QIDP designation for SPR720 for the treatment of lung infections caused by nontuberculous mycobacteria and for the treatment of lung infections caused by *Mycobacterium tuberculosis*. QIDP designation entitles us to priority review of SPR720 for regulatory approval by the FDA. Neither the QIDP nor orphan drug designation, however, guarantee a faster development process or ensure FDA approval.

We believe that our intellectual property portfolio for SPR720 will provide protection globally, including in the United States and Europe, through 2033.

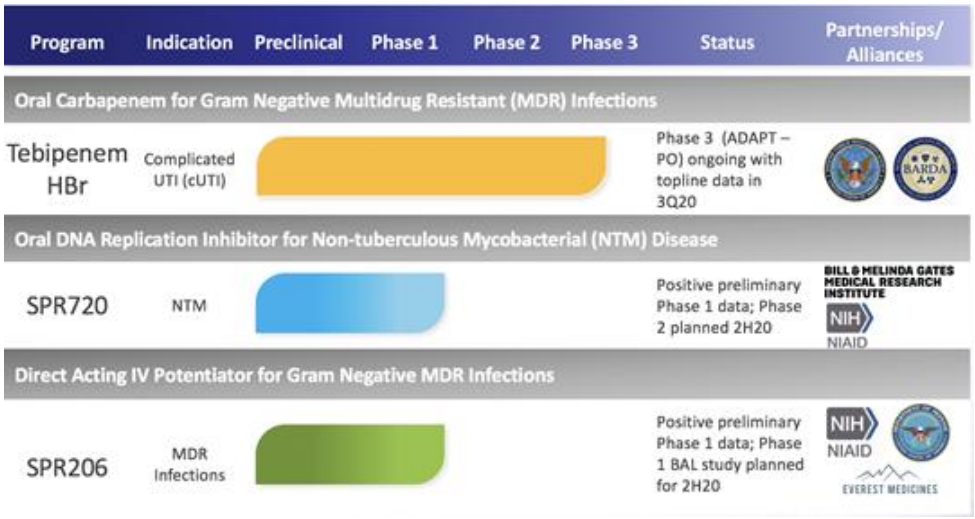
- ***IV Potentiator Product Candidate SPR206: Our Technology Designed to Treat Infections Caused by MDR Gram-Negative Bacteria in the Hospital Setting.*** Our Potentiator Platform is our novel and proprietary technology that we believe will enable us to develop drugs against MDR Gram-negative bacteria. Gram-negative bacteria represent a subset of bacterial organisms distinguished by the presence of an outer cell membrane. SPR206 as an agent from the IV Potentiator Platform is designed to treat MDR Gram-negative bacterial infections through interactions with the bacteria's outer cell membrane as a monotherapy.

  SPR206 is a direct acting IV-administered agent that has demonstrated single-agent antibacterial activity in preclinical studies against Gram-negative bacteria, including organisms identified by the Centers for Disease Control and Prevention, or CDC, and the World Health Organization, or WHO, as urgent and serious threats to human health, including *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. We have completed a preclinical toxicology study of SPR206 in accordance with good laboratory practice, or GLP, requirements. In May 2018, we announced preclinical toxicology and efficacy data that we believe support advancing SPR206 into clinical development. In December 2018, we initiated a Phase 1 clinical trial of SPR206, designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects and in January 2020 we reported a preliminary analysis of the results from the trial. Analysis of preliminary, blinded Phase 1 data suggests that SPR206 is well-tolerated at doses that are likely to be within a therapeutic range for target MDR Gram-negative bacterial infections and has a safety profile that we believe supports the further development of SPR206. The decision to continue development of SPR206 is also supported by data from nonclinical studies in which SPR206 demonstrated activity as a single agent against MDR and extensively drug resistant, or XDR, bacterial strains, including isolates of *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and carbapenem-resistant *Enterobacteriaceae*, in both *in vitro* and *in vivo* models of infection.

  Following an evaluation of the Potentiator Platform product candidates, we have determined to discontinue development of SPR741, effective January 1, 2020, and to move forward with SPR206 as our lead product candidate within the Potentiator Platform. We believe that the collective data from the recent Phase 1 and preclinical studies of SPR206 suggest a potency and safety profile that may be superior to SPR741. Further, we believe SPR206 may have a potentially faster path to pivotal clinical trials when compared with SPR741 because SPR206 is being developed as a single agent. As a result of this decision, we have terminated our license agreement with Northern Antibiotics Oy (Ltd.) relating to SPR741. Effective January 1, 2020, the intellectual property rights associated with SPR741 have entirely reverted to Northern Antibiotics and we no longer have any rights with respect thereto and we no longer have any obligations for the cost of maintaining such intellectual property.

Our Pipeline – Multiple Near-term Catalysts Across the Rare and Infectious Disease Portfolio

The following table sets forth our product candidates, their status and certain anticipated milestones for our product candidates.



Our Strategy

Our goal is to identify, develop and commercialize novel treatments for MDR bacterial infections, focusing on areas of high unmet medical need for safe and effective antibiotic treatments. Key elements of our strategy are as follows:

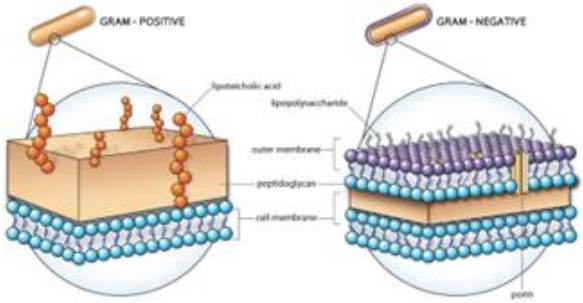
- ***Advance our lead product candidate tebipenem HBr through clinical development and regulatory approval.*** A pivotal Phase 3 clinical trial of tebipenem HBr for the treatment of complicated urinary tract infections (cUTI), ADAPT-PO, continues to enroll patients. ADAPT-PO compares an all oral regimen of tebipenem HBr with ertapenem in approximately 1,200 patients with cUTI or acute pyelonephritis, randomized 1:1 in each treatment arm. In October 2019, an independent review committee issued a positive recommendation to continue the trial using the protocol-defined dose without modification following its analysis of interim pharmacokinetic data from the first 33 patients dosed with tebipenem HBr in the trial. The trial is enrolling well and we continue to expect to report top-line data from the Phase 3 clinical trial in the third quarter of 2020. In addition to cUTI, we believe that tebipenem HBr has the potential to treat other serious and life-threatening infections, including CABP. In addition, our tebipenem HBr collaboration with BARDA, which is further described elsewhere in this Business section, provides funding for a clinical trial in pneumonia patients.
- ***Establish global commercialization and marketing capabilities***. We have global commercialization rights to all of our product candidates, with the exception of tebipenem HBr and SPR206 in certain contractually specified Asian countries. Additionally, the Bill & Melinda Gates Medical Research Institute, or Gates MRI, holds rights to develop SPR720 for the treatment of lung infections caused by Mycobacterium tuberculosis in certain countries. Our management team has significant expertise in the commercialization of infectious disease treatments. Prior to joining us, members of our management team have collectively played leading roles in the approval and launch of 11 infectious disease products. We intend to build a targeted sales force and directly commercialize our product candidates in the United States in both hospital and community settings. Outside the United States, we intend to enter into collaborations with third parties to develop and market our product candidates in targeted geographical markets. By collaborating with companies that have an existing commercial presence and experience in such markets, we believe we can efficiently maximize the commercial potential of our product candidates.
- ***Diversify into rare orphan infectious disease markets such as NTM disease.*** We believe there is a significant opportunity to develop products for underserved “orphan” infectious disease areas, such as NTM disease. These markets offer the attributes of fewer branded or generic competitors as well as chronic therapy. We believe our drug candidate SPR720 has the potential to be the first oral antibiotic approved for the treatment of pulmonary non-tuberculous mycobacterial disease. We may seek to acquire other product candidates for other underserved, debilitating orphan infectious diseases. We intend to continue to advance SPR720 through clinical development. In December 2019, we reported positive preliminary Phase 1 data for SPR720 that suggests SPR720 is generally well-tolerated, with a pharmacokinetic profile that we believe supports further development of the compound as an oral agent for the treatment of NTM disease. In June 2019, SPR720 was the focus of an equity investment by the Novo REPAIR Impact Fund for $10 million as well as a collaboration with Bill & Melinda Gates Medical Research Institute, or Gates MRI, to further the development of SPR720 for tuberculosis, or TB. In March 2020, the FDA granted orphan drug designation for SPR720, a designation given to drugs intended to treat a rare disease or condition that affects fewer than 200,000 persons in the United States. An orphan drug designation can provide specific benefits such as up to seven years of market exclusivity in the United States upon regulatory approval.
- ***Maximize the value of our pipeline through collaborations with other pharmaceutical companies. We may elect to pursue strategic collaborations with other pharmaceutical companies to leverage our Potentiator Platform.*** We believe it may be beneficial to develop and commercialize one or more of our product candidates through partnering opportunities. Such collaborations may include regional collaborations to advance the entire Potentiator Platform, or product-specific deals pairing our product candidates with collaborators’ antibiotics, whether generic or novel, with the intention of enhancing those antibiotics’ performance and efficacy. As part of this strategy, in January 2019, we entered into a license agreement with Everest Medicines to develop, manufacture and commercialize SPR206 in Greater China, South Korea and certain Southeast Asian countries and granted Everest a 12-month exclusive option to negotiate with us for an exclusive license to develop, manufacture or commercialize SPR741 in the same territories. We will continue to seek collaborations to facilitate the capital-efficient development and commercialization of our Potentiator Platform.
- ***Continue to pursue collaborations with non-commercial organizations for scientific expertise and funding support.*** We have received funding support from BARDA, the U.S. National Institute of Allergy and Infectious Diseases, or NIAID, the U.S. Department of Defense, or DoD, and the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, a public-private partnership funded by BARDA within the U.S. Department of Health and Human Services. We intend to continue to collaborate with government agencies and non-profit foundations to support the development of our product candidates. As part of this strategy, in July 2019, we received a $5.9 million award from the DoD in July to fund further clinical development of SPR206.

- ***Expand our portfolio of product candidates for the treatment of MDR infections.*** Since our inception, we have focused on identifying and developing antibiotics to treat MDR infections, and we are using our expertise to aggressively build and expand a portfolio of product candidates for the treatment of such infections where unmet need exists and no viable generic alternatives are available. Our management team has deep-rooted relationships in the academic, medical and corporate infectious disease community, which provide us visibility into new and innovative therapies under development. Our focus in assessing product candidates relies on three principles: 1) broad spectrum of activity, 2) convenient for patients and 3) novel mechanism to overcome resistance. We believe the greatest unmet medical needs for safe and effective antibiotic treatments lie among infections due to MDR bacteria, as patients with these infections often have limited or inadequate therapeutic options, leading to high rates of mortality. The increasing prevalence of drug resistance and MDR bacteria, and the limitations of existing therapies and traditional drug development approaches, highlight the critical need for novel therapies capable of overcoming resistance, particularly orally administrable agents.

The Problem: Increasingly Limited Antibiotic Options for Severe Infections

Antibiotic Background

Antibiotics are drugs used to treat infections that are caused by bacteria. Prior to the introduction of the first antibiotics in the 1930s and 1940s, bacterial infections were often fatal. Today, antibiotics are used routinely to treat and prevent infections. There are two main varieties of bacteria, Gram-negative bacteria and Gram-positive bacteria, which are distinguished by structural differences in their cell envelope. Gram-positive bacteria are surrounded by a single lipid membrane and a thick cell wall, while Gram-negative bacteria are encircled by two lipid membranes, an inner membrane and an outer membrane, with a thinner cell wall in between, as shown in the illustration below.



Antibiotics that target Gram-negative bacteria must be specifically designed to cross both the inner and outer membranes to enter the bacteria. The outer membrane, with its LPS-containing outer leaflet, represents a significant barrier to the entry into the bacteria by antibiotics and is a significant contributor toward reduced potency of many agents in treating Gram-negative bacterial infections. Recent studies have found that Gram-negative bacteria in certain patient types, such as those with sepsis and Interstitial Lung Disease, are associated with higher mortality and increased intensive care unit, or ICU, admission. Moreover, a study of 13,796 patients in intensive care units around the world reported in 2009 that 51% of patients experienced bacterial infections, and of these patients 62% were infected by Gram-negative organisms.

Antibiotics are evaluated according to several criteria, including:

- ***Spectrum***. Antibiotics that are effective against a wide variety of bacteria are considered to be broad-spectrum, while those that act upon only a limited number of bacteria are considered to be narrow-spectrum.
- ***Potency***. Potency is the measure of the microbiological ability of an antibiotic to kill or inhibit growth of bacteria *in vitro*. Potency is commonly expressed as the minimum inhibitory concentration, or MIC, in µg/mL, which is the lowest concentration at which the drug inhibits growth of the bacteria. Antibiotics with lower MICs are considered to be more potent.
- ***Resistance***. Antibiotic resistance refers to the inability of an antibiotic to effectively control bacterial growth. Some bacteria are naturally resistant to certain types of antibiotics. Antibiotic resistance can also occur due to genetic mutations or changes in gene expression. There are numerous mechanisms responsible for antibiotic resistance, and resistance mechanisms are often found together and can be transferred between different bacteria, leading to multi-drug resistance.

Growing Antibiotic Resistance in the Hospital and Community Settings

Antibiotic resistance is one of the largest threats to global health, and resistance rates are increasing. Antibiotic resistance can affect anyone, of any age and in any country. According to the CDC, each year in the United States at least 2 million hospitalized patients become infected with bacteria that are resistant to antibiotics, and at least 23,000 people die each year as a direct result of these infections. Approximately 70% of the pathogens that cause these infections are resistant to at least one drug. Likewise, resistance rates are climbing among community-acquired infections as well. According to van Duin and colleagues in 2016: "Some MDR bacteria have become quite prevalent causes of community-acquired infections. The spread of MDR bacteria into the community is a crucial development, and is associated with increased morbidity, mortality, healthcare costs and antibiotic use." The incidence rate of serious infections is increasing and the proportion of the infections caused by MDR pathogens is increasingly seen as an emerging threat to world health. The CDC estimates that the excess annual cost resulting from these infections in the United States is as high as $20 billion.

According to the CDC, among all of the bacterial resistance problems, Gram-negative pathogens, which cause a majority of all bacterial infections, are particularly worrisome because they are becoming resistant to nearly all drugs that would be considered for treatment. In February 2017, the WHO published a list of Gram- negative bacteria based on the urgency of need for new antibiotics and highlighted a critical group of MDR Gram-negative bacteria that pose a particular threat to human health, including *Acinetobacter*, *Pseudomonas* and multiple Enterobacteriaceae (including *Klebsiella sp.*, *E. coli*, *Serratia* and *Proteus*). These pathogens are associated with significant mortality because the increased incidence of antibiotic resistance has limited the number of effective treatment options.

There is an acute need for new antibiotics to treat MDR bacterial infections, as few new antibiotics capable of addressing such infections have been approved recently for commercialization or are in clinical development. Further, the majority of MDR bacterial infections historically have been acquired in the hospital setting, where they have been treated using IV-administered antibiotics. However, increasingly such infections are being acquired in the community setting, emphasizing the need for orally administrable antibiotics that can effectively treat such infections.

Chronic Bacterial Infection without a Viable Cure

NTM infections represent a growing global health concern and major unmet medical need because of the lack of new medications being developed to combat these bacteria. NTM infections are ubiquitous environmental pathogens that can cause progressive lung damage and respiratory failure, particularly in patients with compromised immune systems or underlying pulmonary disorders.

Although rare, the incidence of pulmonary NTM disease is increasing worldwide. It is estimated that approximately 130,000 patients suffer from NTM disease in the U.S. and Europe, a figure that is growing at a rate of 8% annually. In addition, many patients go undiagnosed and could benefit from treatment with additional testing. The elderly and people with compromised immune or lung function are at greatest risk, as are patients with bronchiectasis for whom it is estimated that up to 50% may also have active lung infection caused by NTM. Treatment of pulmonary NTM disease requires prolonged therapy (continuing for approximately 12 to 24 months) with a combination regimen and is frequently complicated by tolerability and/or toxicity issues. Additionally, there are currently no oral antibiotics specifically approved for use to treat pulmonary NTM disease.

The most common treatment for NTM infections is combination therapy with drugs traditionally used for tuberculosis (TB) which have limited efficacy and high toxicity. NTM infection is also associated with high healthcare costs and high mortality. In 2014, the annual cost in the United States of treating NTM infections alone was estimated at $1.7 billion.

Our Solution

Antibiotics currently used for first-line empiric treatment of MDR acute bacterial infections and NTM infection suffer from significant limitations. We believe that our product candidates will overcome these limitations, as described below:

- ***Tebipenem HBr is designed to address the lack of orally administrable antibiotics to prevent hospitalization and permit IV-to-oral switch therapy in resistant Gram-negative infections***. Resistance to most commonly used classes of oral antibiotics, such as cephalosporins and fluoroquinolones, has increased significantly. Many of the most commonly used antibiotics for MDR Gram-negative infections are only available in an IV-administered formulation. Treatment with effective orally administrable antibiotics may prevent hospitalizations for serious infections and enable earlier, more convenient and cost-effective treatment of patients following hospitalization. Tebipenem HBr is an orally administrable tablet that we believe has the potential, if approved, to treat such infections in both the community and hospital settings, thereby preventing certain hospitalizations and enabling patients to transition to oral treatment. In the community setting, tebipenem HBr, if successfully developed and approved, may allow patients who develop an infection with a resistant pathogen, but are stable enough to be treated in the community, to avoid the need for an IV catheter and even hospitalization. Hospitalization is a key cost driver for hospital systems and payers, with increasing emphasis being placed on hospital avoidance. In the hospital setting, the lack of effective oral stepdown options results in the potential for lengthy hospital stays or the insertion of a peripherally inserted central catheter, or PICC, to facilitate outpatient administration of IV antibiotics. Tebipenem HBr may enable faster discharges, providing cost-saving advantages for the hospital and mitigating the risk of catheter-related infection for patients.

- ***SPR720 is designed to be the first oral treatment for NTM infection where treatment failure is common and no approved therapies exist.*** The current treatment for NTM infection is lengthy and involves combination therapy, often including three or more antibiotics, including injectables. None of these combination treatments are currently approved for use in NTM infection. Treatment failure is common and is often due to poor compliance or patients' inability to tolerate the regimen. Many patients experience progressive lung disease as a result of NTM infection, and mortality rates are high, ranging from 29% to 69% within five years of diagnosis. We believe SPR720, if successfully developed, has the potential to be the first approved oral agent for NTM infection, and it has demonstrated activity *in vitro* and *in vivo* against a range of pathogens, including *Mycobacterium abscessus*, a highly resistant organism causing NTM infection with a high rate of mortality.
- ***SPR206 is designed to address the decline of novel and effective IV-administered antibiotics to treat MDR Gram-negative infections in the hospital setting.*** First-line IV empiric antibiotics, such as levofloxacin, ceftazidime and piperacillin-tazobactam, have experienced diminished utility as the number of bacterial strains resistant to these antibiotics in the hospital has increased. Due to gaps in the spectrum of coverage of antibiotics currently on the market, physicians are often confronted with the need to design complicated multi-drug cocktails for patients with serious infections. Based on results from preclinical studies to date, we believe that SPR206 has the potential to address this need as a single agent.

Our Product Candidates

Tebipenem HBr (tebipenem pivoxil hydrobromide)

Our lead product candidate, tebipenem HBr, is a broad-spectrum oral carbapenem intended for use in adults to treat MDR Gram-negative infections. A pivotal Phase 3 clinical trial of tebipenem HBr for the treatment of cUTI entitled ADAPT-PO continues to enroll patients. This Phase 3 clinical trial compares an all oral regimen of tebipenem HBr with an existing standard of care IV antibiotic, ertapenem, in approximately 1,200 patients with cUTI or acute pyelonephritis, randomized 1:1 in each arm. In October 2019, an independent review committee issued a positive recommendation to continue the trial using the protocol-defined dose without modification following its analysis of interim pharmacokinetic data from the first 33 patients dosed with tebipenem HBr in the trial. The trial is enrolling well and we continue to expect to report top-line data from the Phase 3 clinical trial in the third quarter of 2020. Carbapenems have been utilized for over 30 years and are considered the standard of care for many serious MDR Gram-negative bacterial infections, but to date they have only been available as IV-administered formulations. Currently, there are no commercially available oral carbapenems for use in adults, and we believe tebipenem HBr has the potential to address this unmet need. Tebipenem HBr is an oral tablet formulation of tebipenem. Tebipenem was approved in 2009 in Japan for sale under the name Orapenem for use to treat common infections in pediatric patients. To accelerate our clinical development of tebipenem HBr, in June 2017 we signed an exclusive license to certain data and know-how from Meiji and a global pharmaceutical company, to which we refer as Global Pharma, which we intend to use to support our clinical development of tebipenem HBr. We have global commercialization rights to tebipenem HBr, except in certain contractually specified Asian countries.

The FDA has designated tebipenem HBr as a QIDP for the treatment of cUTI, CABP and DFI under the Generating Antibiotics Incentives Now Act, or the GAIN Act, which enables priority review for regulatory approval by the FDA. If tebipenem HBr is approved for treatment of cUTI, CABP or DFI, the QIDP designation for tebipenem HBr will extend by an additional five years any non-patent exclusivity period awarded for tebipenem HBr in the United States, such as a five-year New Chemical Entity, or NCE, exclusivity granted under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, for a total of 10 years. In Europe, exclusivity for NCEs is 10 years (eight years for data exclusivity and an additional two years for market exclusivity), with the possibility of a one-year extension if the chemical entity is approved for use in an additional indication. Additionally, we believe that our intellectual property portfolio for tebipenem HBr, which includes multiple patent applications pending, will provide tebipenem HBr protection globally, including in the United States and Europe, through 2039.

Advantages of tebipenem HBr

Key attributes of tebipenem HBr, as well as pharmacokinetic data following enrollment of the first 33 patients in our on-going ADAPT-PO pivotal Phase 3 clinical trial, support our confidence in tebipenem HBr's commercial potential, if tebipenem HBr receives regulatory approval. We believe tebipenem HBr has the potential to be a safe and effective treatment for cUTI and other serious and life-threatening infections for which we may develop tebipenem HBr.

- ***Potential to be the first oral carbapenem in adults, if approved***. Tebipenem HBr is designed to be the first broad-spectrum oral carbapenem-class antibiotic for use in adults to treat MDR Gram-negative infections. Unlike other carbapenems, which are only available as IV-administered infusions, tebipenem HBr is an orally administered tablet. Oral administration may potentially allow physicians to avoid IV-administered antibiotics for otherwise healthy or stable patients and/or allow for a reduction in costs associated with avoiding or shortening hospitalization.

- ***Potential for differentiated launch characteristics.*** There are limited branded or generic oral options currently approved or available to treat fluoroquinolone- and cephalosporin-resistant pathogens to assist with transitioning patients from the hospital to the community setting, or to prevent unnecessary hospitalization for cUTI. We believe tebipenem HBr, if approved, to be primarily reimbursable outside the hospital diagnosis-related group, or DRG, system, because of the desire from patients, physicians and payors alike to discharge patients from the hospital. Together, we believe these factors could differentiate tebipenem HBr from other recently launched antibiotic drugs, many of which are injectable, reimbursed within the hospital DRG system, and/or substitutable with equally effective generic alternatives.
- ***Single Phase 3 trial design supported by extensive clinical and preclinical studies; interim PK evaluation supports continuing trial at selected dose.*** Our clinical and preclinical studies with tebipenem HBr suggest that the safety, antimicrobial potency, and pharmacodynamics exposure profile observed to date are comparable to IV carbapenems. Data from our Phase 1 clinical trial of tebipenem HBr studying a dosage of 600 mg three times per day (TID) have suggested a tolerability profile and pharmacodynamic activity in plasma and urine for tebipenem HBr that are comparable to available data for IV-administered ertapenem given once daily. Data from Meiji's Phase 2 dose ranging study of tebipenem pivoxil in cUTI show microbiological eradication at test of cure comparable to other IV agents for cUTI. Also, the *in vitro* potency of tebipenem HBr against Enterobacteriaceae was observed to be similar to IV-administered ertapenem and imipenem in preclinical studies. As a result of this extensive existing data, we believe that tebipenem HBr has the potential to be used for the treatment of cUTI and other serious and life-threatening infections caused by resistant Gram-negative pathogens.
- ***Favorable safety, efficacy and tolerability profile suggested by clinical trials of tebipenem in Japanese populations***. A granule formulation of tebipenem has been approved for use in Japan in pediatric patients since 2009, where it has demonstrated a favorable safety and efficacy profile. Approximately 1,200 subjects were dosed with the active pharmaceutical ingredient of tebipenem HBr, tebipenem, in clinical and pharmacologic studies during development of this drug by Meiji and its partner in Japan. This data set includes 741 adults, including 88 patients with cUTIs, the initial indication for which we are developing tebipenem HBr. In each case tebipenem has demonstrated a favorable safety, pharmacokinetic and tolerability profile. In addition, Meiji has conducted a 3,540 patient post-marketing study supporting the safety and tolerability profile of tebipenem, specifically demonstrating a safety profile that aligns well with that observed across the clinical trial program and tolerability in line with other broad spectrum oral antibiotics.
- ***Potential to enable IV-to-oral transition of antibiotic treatment to assist with reduction in hospital stays and/or eliminate the need for hospitalization.*** We believe the unique oral formulation of tebipenem HBr may enable patients who begin IV-administered treatment for ESBLs in the hospital setting to transition to oral dosing of tebipenem HBr either in the hospital or upon discharge for convenient home-based care. We believe that the availability and use of an oral carbapenem as a transition therapy may eliminate hospitalization or reduce the length of a patient's hospital stay and the overall cost of care.

We believe the foregoing advantages of tebipenem HBr also significantly differentiate tebipenem HBr from fluoroquinolones. Fluoroquinolones are the most widely used antibiotic class in treating community and hospital Gram-negative infections, but they have encountered increasing resistance among MDR Gram-negative bacteria and are associated with significant adverse effects. The table below reflects resistance rates in the United States in the community and hospital settings.

cUTIs in the United States	**2013-2014 *E. coli* Resistance Rates to Fluoroquinolones**	**2000-2004 *E. coli* Resistance Rates to Fluoroquinolones**
Community Setting	11.7%	0%
Hospital Setting	34.5%	3.5%

Currently, fluoroquinolones are the most frequently selected antibiotic for empirical urinary tract infection, or UTI, treatment in the community and hospital settings. Current UTI treatment guidelines published by the Infectious Diseases Society of America identify fluoroquinolones as an appropriate empirical therapy option. This recommendation, however, is contingent on local resistance rates being less than 10%. The endemicity (high rates) of fluoroquinolone-resistant *E. coli* found in the United States today in the community and hospital settings based on the table above would suggest that fluoroquinolones should not be used empirically for cUTI patients.

The following table highlights the observed *in vitro* potency differences between tebipenem HBr and levofloxacin, the most widely used fluoroquinolone. As shown below, tebipenem HBr has a MIC90 value of 0.03 µg/ mL, which compares favorably (i.e., at or below) to the potency value obtained by levofloxacin.

Compound	*E. coli* MIC_{90} (µg /mL)
tebipenem HBr	0.03
Levofloxacin	>4

In addition, the FDA has issued several warnings against the use of fluoroquinolones in certain patients. In particular, an FDA Advisory Committee stated in November 2015 that the risk of serious side effects caused by fluoroquinolones generally outweighs the benefits for patients with acute bacterial sinusitis, acute exacerbation of chronic bronchitis and uncomplicated UTIs. The FDA has determined that fluoroquinolones should be reserved for use in patients with these conditions who have no alternative treatment options. We believe tebipenem HBr could become a potential alternative to oral fluoroquinolones based on its safety and efficacy profile.

Significant Market Opportunity for tebipenem HBr

Given the observed activity of tebipenem HBr against different bacteria, we view the market opportunity for tebipenem HBr, if approved, to be substantial, including for the following uses:

- Community setting: Treating urinary tract infections acquired in the community setting without the need for patient hospitalization.
- Hospital setting: Transitioning patients hospitalized for UTIs to an appropriate oral therapy as they are discharged from the hospital.

UTIs are among the most common bacterial diseases worldwide, with significant clinical and economic burden. IQVIA (formerly QuintilesIMS) estimates that between 33 and 34 million patients either visit their physician or are hospitalized for a UTI or otherwise suspected of experiencing a UTI in the United States annually. While drugs such as trimethoprim/sulfamethoxazole (Bactrim/Septra) and fluoroquinolones (levofloxacin, ciprofloxacin) have been the primary oral options for treatment of UTIs caused by Gram-negative organisms, nearly 30% to 35% of UTIs are resistant, which has led to increased use of IV-administered therapeutics such as carbapenems.

IQVIA completed a market assessment in August 2017 in the community and hospital settings in which it estimated that there were 11 to 12 million patients annually who presented in the community physician's office with a UTI and 3.5 to 4.5 million patients annually in the hospital with a UTI in the United States alone. Of these UTIs, 10 to 11 million are suspected to be caused by Gram-negative bacteria, and 4 to 5 million of these patients had an infection that is resistant to or failed first-line therapy, such as the fluoroquinolone class, or require IV therapy due to the severity of infection. Physicians in the survey reported high concern with growing fluoroquinolone resistance and lack of oral options for MDR Gram-negative infections. We believe tebipenem HBr is well positioned to meet the unmet need for an oral therapy for community-acquired UTI and may offer physicians an option for treating MDR UTIs while avoiding patient hospitalization. In addition, we believe tebipenem HBr has the potential to accelerate hospital discharge and obviate the need for continued IV-administered therapy at home by transitioning discharged patients to an at-home oral therapy. ADAPT-PO, our ongoing pivotal Phase 3 clinical trial for tebipenem HBr, is focused on patients who suffer from a subset of UTIs called cUTIs, which affect approximately 4.9 million patients in the United States annually. A significant majority of UTIs, including cUTIs, are caused by a group of MDR Gram-negative bacteria called Enterobacteriaceae.

Tebipenem HBr Clinical Development Program

Single Pivotal Phase 3 Clinical Trial (ADAPT-PO)

We initiated a Phase 1 dose-selection clinical trial of tebipenem HBr in healthy volunteers in Australia in October 2017. In September 2018, we announced positive results from the final analysis of this study and identified a dose of 600 mg TID for our planned single pivotal Phase 3 clinical trial of tebipenem HBr in cUTI. Based on our pre-IND, pre-Phase 3 meeting with the FDA, we believe that positive results from a single pivotal Phase 3 clinical trial of tebipenem HBr in cUTI demonstrating a 10% non-inferiority margin would support the approval of tebipenem HBr for the treatment of cUTI. As a result of the meeting, we submitted an IND application for tebipenem HBr in cUTI with the FDA and received FDA acceptance of the IND application in February 2019. We then initiated the single pivotal Phase 3 clinical trial required for approval of tebipenem HBr in cUTI entitled ADAPT-PO. We opened clinical trial sites in April 2019 for the Phase 3 trial and are actively enrolling patients. The pivotal Phase 3 clinical trial is designed as a double-blind, double-dummy trial to compare oral tebipenem HBr with an existing standard of care IV antibiotic, ertapenem, in approximately 1,200 patients with cUTI or acute pyelonephritis, randomized 1:1 in each arm. In October 2019, an independent review committee issued a positive recommendation to continue the trial using the protocol-defined dose without modification following its analysis of interim pharmacokinetic data from the first 33 patients dosed with tebipenem HBr in the trial. The trial is enrolling well and we expect to report top-line data from the Phase 3 clinical trial in the third quarter of 2020. Following receipt of top-line data from our ADAPT-PO Phase 3 clinical trial of tebipenem HBr, if favorable, together with requisite safety data, drug-drug interaction studies and other studies, we intend to submit to the FDA an NDA for tebipenem HBr to treat cUTI, including acute pyelonephritis. These data, if positive, may also support marketing applications in other global regions.

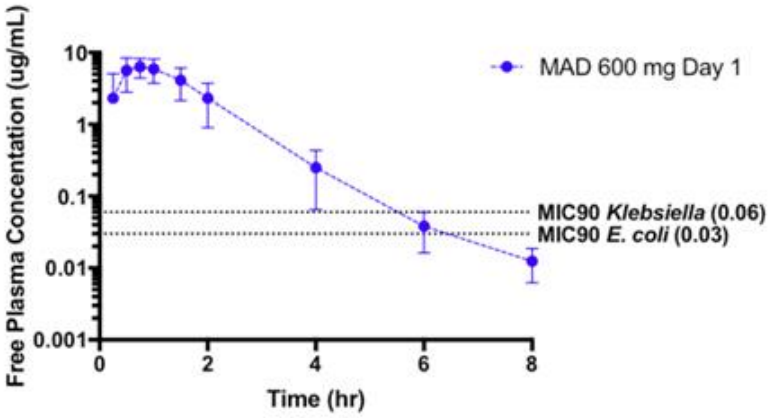
QIDP Designation

The FDA has designated tebipenem HBr as a QIDP for the treatment of cUTI, CABP and DFI under the GAIN Act, which enables priority review for regulatory approval by the FDA. The QIDP designation for tebipenem HBr, however, does not guarantee a faster development process or ensure FDA approval. Further, if tebipenem HBr is successfully developed and approved for the treatment of cUTI, CABP or DFI, the FDA's QIDP designation for tebipenem HBr should extend any non-patent exclusivity period awarded to tebipenem HBr in the United States for five years, such as a five-year New Chemical Entity data exclusivity granted under the Hatch-Waxman Act.

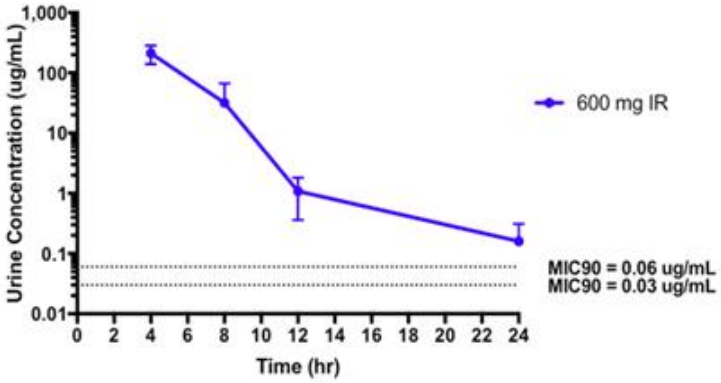
Phase 1 Clinical Trial Results

Our completed Phase 1 SAD and MAD clinical trial of tebipenem HBr assessed the safety, tolerability and pharmacokinetics of orally administered tebipenem HBr. The Phase 1 clinical trial enrolled 124 healthy adult volunteers into 14 SAD cohorts with tebipenem HBr given orally as single doses ranging from 100 mg to 900 mg daily and two MAD cohorts with tebipenem HBr given orally at doses of 300 mg and 600 mg every 8 hours (TID administration) for 14 days. Repeated dose administration of both 300 mg and 600 mg of tebipenem HBr TID was well tolerated, with a safety profile consistent with the carbapenem class of antibiotics. Final results demonstrated a linear and proportional increase in plasma exposure over the dose range tested, with no accumulation over 14 days of repeated dosing. Furthermore, the administration of tebipenem HBr in the fed or fasting state did not substantially alter the plasma drug exposure, indicating that tebipenem HBr can likely be administered without regard to meals. Consistent with the predominantly renal elimination of tebipenem HBr, peak urine concentrations were approximately 50 to 100-fold higher than maximum concentrations in plasma, as shown in the charts below, supporting tebipenem HBr's potential utility as a treatment for patients with cUTI.

Free Plasma Concentrations of tebipenem HBr



Urine Concentration of tebipenem HBr after a Single Dose



We also plan to conduct routine ancillary clinical pharmacology studies in parallel with the Phase 3 trial as required by the FDA for the approval of tebipenem HBr, including a renal insufficiency study, a thorough QT prolongation study and a drug-drug interaction study.

In vitro Activity Against MDR Enterobacteriaceae

Tebipenem HBr has shown activity in preclinical *in vitro* studies against a wide variety of ESBL-producing *E. coli* and ESBL-producing K. pneumoniae strains. We believe these data show the ability of orally available tebipenem HBr to deliver similar activity to comparative IV-administered agents.

Approximately 1,200 subjects have been dosed with tebipenem pivoxil in clinical and pharmacologic studies during the development of this drug by Meiji in Japan. The data set from these studies includes 741 adults, including 88 patients with cUTIs, the initial indication for which we plan to develop tebipenem HBr. In addition, there are post-marketing outcomes data reporting the safety and efficacy of tebipenem in 3,540 pediatric patients with pneumonia, otitis media, or sinusitis. These data are consistent with the safety profile of tebipenem as established in the clinical trial. We have also tested tebipenem HBr *in vitro* and in animal models. We believe that nonclinical assays are generally predictive of clinical efficacy for antibiotics, particularly in the case of a well-understood class such as carbapenems.

Meiji Phase 2 Clinical Trial Data of Tebipenem in cUTI

Meiji and its partner conducted two exploratory, dose-ranging Phase 2 clinical trials of tebipenem in patients with cUTI including patients with acute pyelonephritis. These trials were conducted in Japan between 2001 and 2004. Study L-084 04 (report date 2003), a multicenter open-label study to evaluate the efficacy (clinical and microbiological) and safety (adverse events and laboratory tests) of tebipenem pivoxil at doses of 100 mg administered TID (Group A), 150 mg administered BID (Group B), and 150 mg administered TID (Group C), for seven days in patients with cUTI. There were 51 adult patients, aged 20-74 years inclusive, enrolled with 40 being evaluable for efficacy (14 in Group A; 17 in Group B; 9 in Group C). Study ME1211 (report date 2004), a multicenter, open-label study to evaluate efficacy (early and late assessments) and safety (adverse events and laboratory tests) of tebipenem pivoxil at doses of 250 mg administered BID (500 mg Group) and 300 mg administered TID (900 mg Group) for seven days in patients with UTI. There were 37 adult patients, aged 20 to 74 years inclusive, enrolled with all being evaluable for efficacy (19 in 500-mg Group; 18 in 900-mg Group). In these studies, dosing three times per day showed the greatest effect as compared with other dosing regimens, consistent with the interim results from our Phase 1 clinical trial.

Although the design of the Phase 2 clinical trials in Japan was different from what is recommended in FDA guidance for clinical trials in patients with cUTI, including acute pyelonephritis, we believe these results provide support for our planned single pivotal Phase 3 clinical trial of tebipenem HBr at a dose of 600 mg TID for the treatment of cUTI. With respect to these results, which are summarized in the chart below, the efficacy rate refers to the proportion of subjects judged to have experienced a “markedly effective” or “effective” tebipenem dosage versus the total number of subjects tested, and the negative conversion rate refers to the proportion of subjects with negative urine cultures versus the total number of subjects tested.

Observed Efficacy of Tebipenem Pivoxil in Meiji Phase 2 Trials in UTI

Study L-084 04

	Subjects	Efficacy Rate*	Negative Conversion Rate
300-mg group A (100 mg administered TID)	14	92.9%	92.9%
300-mg group B (150 mg administered BID)	17	94.1%	94.1%
450-mg group C (150 mg administered TID)	9	100%	100%

* Based on overall clinical outcome.

Study ME1211

	Subjects	Early Efficacy Assessment*	Negative Conversion Rate**
500-mg group A (250 mg administered BID)	16	93.8%***	87.5%
900 mg group B (300 mg administered TID)	16	93.8%	93.8%

* Based on overall clinical effect at the end of therapy.

** Early assessment, at end of therapy. For the purpose of this assessment, negative conversion rate is defined as the rate of subjects with negative urine cultures.

*** “Markedly effective” or “effective.”

In these two Phase 2 cUTI trials, 83-84% of patients had complicated lower tract UTIs (complicated cystitis). Taken together, the Meiji Phase 2 trials assessed the clinical and microbiological response to doses of tebipenem pivoxil ranging from 300 mg to 900 mg per day administered as two (BID) or three (TID) split doses. Clinical and microbiological responses at end of therapy, or EOT, were high for all regimens tested; however, the microbiological eradication rates at test of cure, or TOC, were highest in patients receiving tebipenem 150 mg or 300 mg TID. Of note, the microbiological eradication rates at the TOC in these dosing groups was similar to that reported for the subsets of patients with complicated cystitis in recent cUTI clinical trials utilizing intravenously administered antibiotics. Of note, the AUC exposure observed with 600 mg oral TID of tebipenem HBr in in our single- and multiple-ascending dose study was comparable to that demonstrated to be effective in the Meiji cUTI trials. The appropriateness of the proposed therapeutic dose of tebipenem HBr is supported by a pharmacokinetic/pharmacodynamic analysis based on three preclinical pharmacodynamic models (murine neutropenic thigh, hollow fiber, and one compartment pharmacodynamic model) and a clinical population pharmacokinetic model, which indicates that 600 mg of tebipenem HBr administered TID is likely to achieve high target attainment over the MIC range of the most prevalent Enterobacteriaceae causing cUTI.

Japanese Data Supporting Safety of Tebipenem

Tebipenem pivoxil is a prodrug that is metabolized to tebipenem, its therapeutically active form. We view the clinical safety profile of tebipenem pivoxil established by Meiji as relevant and supportive of tebipenem HBr because both metabolize to the active metabolite, tebipenem, in plasma. Our formulation development efforts are designed to improve target concentration while maintaining the exposure per dose.

Tebipenem pivoxil is an orally administered carbapenem, which is a sub-group of the beta-lactam class of antibiotics. The safety of tebipenem pivoxil was evaluated in approximately 1,200 subjects supporting the application for approval in Japan. In this safety data set, there are 741 adult subjects across 17 trials and 440 pediatric subjects across six trials. These 23 trials in total, included one double-blind, comparator-controlled trial in children, five open-label trials in children, five trials enrolling adult patients (including two open-label cUTI trials), and 12 Phase 1 clinical pharmacology trials. Among the pharmacology trials, tebipenem pivoxil was studied for an effect on QT interval, and for the known effect of the pivoxil prodrug on plasma carnitine concentrations.

In these studies, tebipenem pivoxil was generally well tolerated, with an adverse event, or AE, profile comparable to common, approved oral beta lactam antibiotics and IV-administered carbapenems. The most common AEs were gastrointestinal (e.g., diarrhea, loose stools) in both children and adults, and in the Phase 3 clinical trial of otitis media, the incidence was similar to that reported for the comparator, cefditoren pivoxil, an oral cephalosporin antibiotic. No effect of the administration of tebipenem pivoxil on the prolongation of the QT interval was observed, and the effect on plasma carnitine concentrations was reversed post treatment and not associated with AEs. A side effect seen with beta-lactam antibiotics is seizures; however, there have been no reports of inducement of seizures due to the administration of tebipenem pivoxil in clinical trials.

Meiji has reported post-marketing outcomes data reporting the safety and efficacy of Orapenem Fine Granules 10% for Pediatric Use (tebipenem pivoxil) in pediatric patients with pneumonia, otitis media, or sinusitis. A total of 3,547 cases were enrolled into the observational study, and the analysis was conducted using 3,540 cases for which it was possible to recover the questionnaires.

A total of 348 instances of adverse drug reactions were observed in 334 cases amongst the 3,337 cases (including 6 adult cases) used in the safety analyses, and the incidence of adverse drug reactions was 10.01% (334 cases/3,337 cases). The adverse drug reaction that occurred most frequently was “diarrhea” (9.5%, 318 instances/3,337 cases). One serious drug reaction was observed of “multi-organ failure”. These data are consistent with the safety profile of tebipenem as established in the pediatric clinical trials and reflected in the Orapenem product labeling in Japan.

A clinical trial evaluating the effect of tebipenem pivoxil dosing over one week on intestinal flora was also performed. Total aerobic and anaerobic bacterial counts were evaluated. Total bacterial count was reduced by day 7 of the study in both the 100 and 200 mg TID groups. However, no additional change in bacterial count was observed on subsequent examination days. Neither fecal *C. difficile* nor its toxin was detected in any of the subjects during or following completion of the 7-day dosing period.

Funded Label Expansion Opportunity

In addition to cUTI, we believe that tebipenem HBr has the potential to treat other serious and life-threatening infections, including CABP. Our BARDA award provides funding for Phase 1 and Phase 2 trials supporting a potential CABP indication for tebipenem HBr.

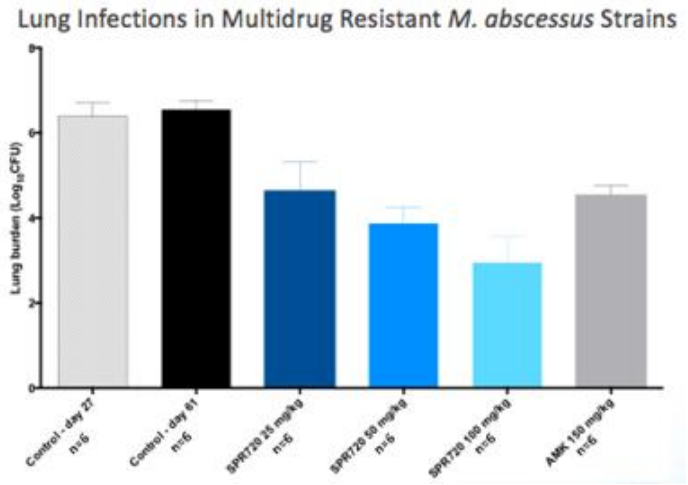
SPR720 Pulmonary Non-Tuberculous Mycobacterial (NTM) Disease Program

A second area of our focus is rare infectious diseases, specifically non-tuberculous mycobacterial disease. We are developing SPR720, a therapeutic candidate with a novel mechanism of action for the treatment of NTM disease. NTM causes chronic and serious lung disease with debilitating symptoms that leads to a decline in lung function. It can have a significant physical and emotional impact on patients. SPR720 is designed to be the first novel, oral candidate to treat pulmonary NTM disease. SPR720 represents a novel class of antibacterial agents that target enzymes essential for bacterial DNA replication.

SPR720 has several key attributes including:

- ***Broad spectrum of activity.*** SPR720 has demonstrated a broad spectrum of activity in preclinical studies against the most common organisms causing NTM infections, including *Mycobacterium avium* complex, or MAC, *Mycobacterium kansasii* and *Mycobacterium abscessus*. SPR720 is applicable to both non-refractory and refractory patients.
- ***Convenient for patients.*** SPR720 has high oral bioavailability. Many patients can find inhalers difficult to use and poor inhalation technique can negatively impact drug delivery and response to therapy. Oral therapy is simple and more convenient.
- ***Novel mechanism.*** SPR720 employs a novel mechanism and has no known cross-resistance with marketed antibiotics. Recent studies have shown the high prevalence of drug resistance in NTM infection species that threatens adequate control of the disease. Novel mechanisms may help evade existing modes of resistance.
- ***Lung exposure.*** SPR720 is an oral drug that penetrates the pulmonary space. A bronchoalveolar lavage study in non-human primates supports lung exposure. Furthermore, macrophage data from a 28-day hollow-fiber model of infection demonstrates intracellular and extracellular activity of the drug.

SPR720 has shown potent activity against most common NTM infection species, such as *M. avium*, *M. abscessus* and *M. kansasii*. As shown in the exhibit below, SPR720 showed dose responsive activity against difficult to treat MDR pathogens, with better activity as compared to amikacin (AMK) considered one of the positive controls in this experiment.



Non-tuberculous mycobacteria are typically found in water and soil. NTM infections cause a rare infection of the lung that is acquired through inhalation of this microbe. There are approximately 150 types of mycobacteria, with MAC and Mycobacterium abscessus the most common cause of NTM infections, together comprising almost 90% of all NTM infections.

NTM disease occurs in many different types of patients. NTM disease often occurs in people with compromised immune systems, such as those with HIV, or those with respiratory conditions such as cystic fibrosis, chronic obstructive pulmonary disease, asthma or bronchiectasis. According to Strollo et al. and Adjemian et al., the diagnosed patient population is approximately 86,000 in the United States. The annual prevalence of NTM disease is increasing at an estimated rate of 8% per year. While people of any age can be infected by NTM, it mostly affects middle-aged to elderly adults, and is increasing among patients over 65, a population expected to nearly double by 2030. While relatively rare compared to other infectious diseases, the prevalence of NTM disease has more than doubled since 1997 and unfortunately, infections caused by NTM are often undiagnosed, masquerading as another respiratory condition such as COPD or asthma. By comparison, the prevalence of tuberculosis in North America has declined.

There are currently no oral FDA-approved therapeutics specifically approved for use to treat NTM disease. Given the unmet medical need, there are regulatory incentives available to encourage drug development to address NTM disease. These include orphan drug designation, potential for breakthrough therapy status and QIDP designation. Treatment of NTM disease requires prolonged therapy (continuing for approximately 12 to 24 months) with a combination regimen and is frequently complicated by tolerability and/or toxicity issues. Treatment failure is common and is often due to poor compliance or inability to tolerate the regimen. Many patients experience progressive lung disease and mortality is high. We believe there is a need for new, potent, orally available therapies for NTM disease. While there are competitive compounds in development for NTM disease, these therapies are not effective in all patients and are not orally available.

We believe that our intellectual property portfolio for SPR720, which includes multiple issued patents and patent applications pending, will provide SPR720 protection globally, including in the United States and Europe, through 2033.

Our SPR720 Development Plan

Our strategy is to develop SPR720 to become the first oral treatment FDA-indicated for NTM disease, and to enable refractory patients to regain a better quality of life. SPR720 is currently in clinical development. We initiated a Phase 1 clinical trial of SPR720 in January 2019, designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects. Preliminary analysis of blinded data from this Phase 1 trial suggests that SPR720 is generally well-tolerated, with a PK profile that we believe supports the further development of SPR720 as an oral agent for the treatment of NTM pulmonary disease. We expect to present final data from the SPR720 Phase 1 SAD/MAD clinical trial in 2020 at a medical meeting. We plan to request a meeting with the FDA in the first half of 2020, submit an IND to the FDA in the second half of 2020 and, following IND acceptance, initiate a dose-ranging Phase 2a clinical trial evaluating SPR720 in patients with NTM disease due to *Mycobacterium avium* complex, or MAC, in the second half of 2020.

The Phase 1 clinical trial of SPR720 evaluated the safety, tolerability and PK of orally administered SPR720 at single doses ranging from 100 mg to 2000 mg and repeat total daily doses ranging from 500 mg to 1500 mg for up to 7 to 14 days. Across seven SAD and five MAD cohorts, a total of 96 healthy volunteers (including a cohort of healthy elderly (age ≥ 65 years) volunteers) were randomized to receive SPR720 or placebo. There were no serious adverse events reported and all participants completed the trial. An analysis of preliminary blinded data indicates that SPR720 was generally well-tolerated at doses up to 1000 mg over the maximum studied duration of 14 days. Preliminary analyses of PK data across the cohorts show no significant impact of either advanced age or administration with food on PK variables. At doses of 500 mg or higher, the mean plasma drug exposures of SPR719, the active metabolite of SPR720, are consistent with those suggested by *in vivo* models of SPR720 to be necessary for clinical efficacy against target NTM pathogens.

Our IV Potentiator Product Candidate SPR206

SPR206 is a product candidate from our IV Potentiator Platform in development as an innovative option to treat Gram-negative infections in the hospital setting. SPR206 has exhibited *in vitro* and *in vivo* activity against Gram-negative bacteria, including organisms identified by the CDC and the WHO as urgent and serious threats to human health. Specifically, in nonclinical studies SPR206 demonstrated activity as a single agent against MDR and XDR bacterial strains, including isolates of *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and carbapenem-resistant *Enterobacteriaceae*, in both *in vitro* and *in vivo* models of infection.

In December 2018, we initiated a Phase 1 clinical trial of SPR206, designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects, and we reported positive preliminary data from the trial in January 2020. The analysis of preliminary, blinded data from the Phase 1 double-blind, placebo-controlled single ascending dose (SAD) and multiple ascending dose (MAD) clinical trial in healthy adult volunteers suggests that SPR206 is well-tolerated at doses that are likely to be within a therapeutic range for target MDR Gram-negative bacterial infections and has a safety profile that we believe supports continuing development of the product candidate. A total of 96 healthy volunteers were randomized to receive SPR206 or placebo. All reported adverse events were mild to moderate and there were no reported severe or serious adverse events. No evidence of nephrotoxicity was observed and there were no subjects with clinically significant changes in laboratory tests during the study. Although the data remain blinded, an analysis of preliminary data indicates that SPR206 was well-tolerated at doses up to 100 mg administered three-times a day, a total of 300 mg daily, for 14 consecutive days. Preliminary analyses of pharmacokinetic data across the cohorts indicates dose linearity and dose proportionality as well as mean plasma drug exposures of SPR206 that are concordant with preclinical models predictive for clinical efficacy against target Gram-negative pathogens.

We plan to conduct a Phase 1 bronchoalveolar lavage (BAL) clinical trial assessing the penetration of SPR206 into the pulmonary compartment as well as initiate a renal impairment study of SPR206 in the second half of 2020.

SPR206 has been granted QIDP designation by the FDA for the treatment of cUTI and hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP). We have multiple patent applications pending for SPR206 that we believe will provide SPR206 protection globally, including in the United States and Europe, through 2039.

Following an evaluation of the IV Potentiator Platform product candidates, we have determined to discontinue development of SPR741, effective January 1, 2020, and to move forward with SPR206 as our lead product candidate within the Potentiator Platform. We believe that the collective data from the recent Phase 1 and preclinical studies of SPR206 suggest a potency and safety profile that may be superior to SPR741. Further, we believe SPR206 may have a potentially faster path to pivotal clinical trials when compared with SPR741 because SPR206 is being developed as a single agent. As a result of this decision, we have terminated our license agreement with Northern Antibiotics Oy (Ltd.) relating to SPR741. Effective January 1, 2020, the intellectual property rights associated with SPR741 have entirely reverted to Northern Antibiotics and we no longer have any rights with respect thereto and we no longer have any obligations for the cost of maintaining such intellectual property.

SPR206 Advantages

We believe that the following key attributes of SPR206, an agent from our Potentiator Platform, generally has the potential to support the clinical utility and commercial value of our Potentiator Platform for the safe and effective treatment of serious Gram-negative infections:

- ***Potential to Expand the Potency of Standard-of-Care Antibiotics***. Products within the Potentiator Platform were designed to expand the potency of standard-of-care antibiotics by restoring and expanding their Gram-negative activity. We believe that this novel mechanism could provide a new option for patients with resistant Gram-negative infections, thereby improving therapeutic outcomes, decreasing physicians' reliance on older poorly tolerated and ineffective drugs.
- ***SPR206 appears to be a safe and potent IV-administered direct-acting agent***. SPR206 is designed to interact with LPS to disrupt the outer membrane. SPR206 is also designed to have direct antibiotic activity, while retaining Potentiator activity, including activity against *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Data from SPR206 *in vitro* and *in vivo* GLP safety pharmacology and absorption, distribution, metabolism, and excretion, or ADME, studies and 14-day, two-species GLP toxicology studies provide support for an acceptable safety profile, which led to SPR206's designation as a clinical candidate and the initiation of a Phase 1 clinical trial in December 2018. Preliminary Phase 1 data demonstrate that SPR206 is well-tolerated at doses that are likely to be within a therapeutic range for target MDR Gram-negative bacterial infections and has a safety profile that we believe supports the further development of SPR206. We are developing SPR206 as a treatment for high-risk patients with suspected or known Gram-negative infections such as carbapenem-resistant *Enterobacteriaceae*, or CRE, carbapenem resistant *Acinetobacter baumannii*, or CRAB, and MDR *Pseudomonas aeruginosa*, or MDR PA, to prevent mortality and reduce the length of stay in the hospital setting.

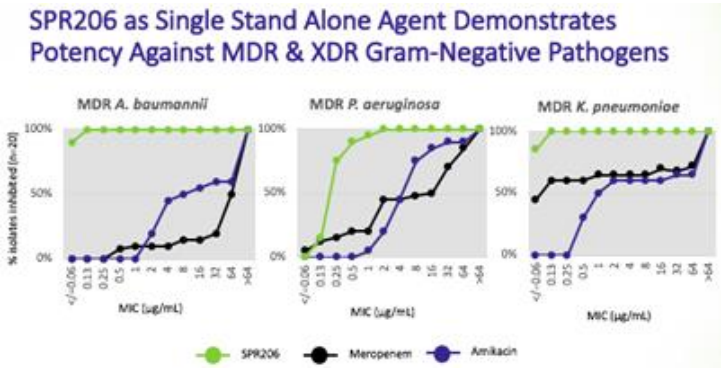
SPR206—Development Plan

Positive Phase 1 Preliminary data for SPR206

In December 2018, we initiated a Phase 1 trial of SPR206, designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects. The trial evaluated the safety, tolerability and pharmacokinetics of intravenously administered SPR206 at single doses ranging from 10 mg to 400 mg in seven SAD cohorts and repeat total daily doses ranging from 75 mg to 450 mg for seven consecutive days and 300 mg for 14 consecutive days across five MAD cohorts. A total of 96 healthy volunteers were randomized to receive SPR206 or placebo. Preliminary data of the blinded data in January 2020 indicated that SPR206 was well-tolerated at doses up to 100 mg administered three-times a day, a total of 300 mg daily, for 14 consecutive days. All reported adverse events were mild to moderate and there were no reported severe or serious adverse events. No evidence of nephrotoxicity was observed and there were no subjects with clinically significant changes in laboratory tests during the study. Preliminary analyses of pharmacokinetic data across the cohorts indicates dose linearity and dose proportionality as well as mean plasma drug exposures of SPR206 that are concordant with preclinical models predictive for clinical efficacy against target Gram-negative pathogens.

In Vitro Activity of SPR206 against MDR Gram-Negative Bacteria

Results from multiple susceptibility studies against contemporary clinical isolates suggest that SPR206 possesses potent activity against MDR Enterobacteriaceae, carbapenem resistant *Pseudomonas aeruginosa* and carbapenem resistant *Acinetobacter baumannii*.



Collaboration and License Agreements

In addition to our own patents and patent applications, we have acquired or licensed patents, patent applications and know-how from various third parties to access intellectual property covering product candidates that we are developing. We have certain obligations under these acquisitions or licensing agreements, including diligence obligations and payments, which are contingent upon achieving various development, regulatory and commercial milestones. Also, pursuant to the terms of some of these license agreements, when and if commercial sales of a product commence, we may be obligated to pay royalties to such third parties on net sales of the respective products. Some of our license agreements include sublicenses of rights owned by third-party head licensors. In addition, we have entered into a license agreement (described below) pursuant to which we have granted certain development, manufacturing and commercialization rights with respect our Potentiator product candidates.

Meiji Agreements

To support our development of tebipenem HBr, in June 2017 we entered into an exclusive License Agreement with Meiji Seika Pharma Co., Ltd., or the Meiji License. Pursuant to the Meiji License, we obtained know-how, data and regulatory documents that will support the development of tebipenem HBr.

We retain exclusive rights to commercialize tebipenem HBr throughout the world, except in Japan, Bangladesh, Brunei, Cambodia, China, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, South Korea, Taiwan, Thailand and Vietnam, where Meiji will have exclusive rights to commercialize tebipenem HBr. With Meiji, we have established a joint development committee for the management of the development of tebipenem HBr, including any joint, cross-territory studies that may be undertaken by the parties, if any. In addition, the parties will establish a joint commercialization committee to coordinate information sharing relative to commercialization of the new formulation.

Meiji and we have granted each other exclusive cross licenses to our respective tebipenem intellectual property, including know-how and regulatory documentation. The license granted to us by Meiji includes certain know-how that Meiji received from Global Pharma, as described below. As such, our rights to the Global Pharma know-how component are non-exclusive.

Under the Meiji License, we have paid Meiji a one-time nonrefundable upfront fee of $0.6 million and are obligated to pay Meiji future clinical and regulatory milestone payments up to an aggregate of $3.0 million and royalties of a low single-digit percentage based on net sales of tebipenem HBr. In October 2017, we paid a $1.0 million milestone payment to Meiji upon the enrollment of the first patient in our Phase 1 clinical trial of tebipenem HBr. Additionally, we are obligated to pay Meiji a percentage of certain amounts received from any sublicensees, up to an aggregate of $7.5 million.

Some of the know-how that we received under the Meiji License to support tebipenem HBr development was originally obtained by Meiji through a license from Global Pharma, which we refer to as the head license. Prior to entering into the Meiji License with us, Meiji received written approval from Global Pharma permitting Meiji to enter into the Meiji License with us. Specifically, in a letter agreement between Global Pharma and Meiji entered into in January 2017, Global Pharma consented to Meiji assisting us with the transfer or license of the Global Pharma know-how and Meiji know-how on a non-exclusive basis outside of those Asian countries identified above, as well as certain related matters. This letter agreement does not contemplate us having any right to sublicense the Global Pharma know-how. Global Pharma retains rights to its know-how outside of those Asian countries identified above.

The Meiji License continues in effect until the expiration of all payment obligations thereunder (including royalty payments and licensee revenue) on a product-by-product and country-by-country basis, unless earlier terminated by the parties. Pursuant to the terms of the Meiji License, in addition to each party's right to terminate the agreement upon the other party's material breach (if not cured within a specified period after receipt of notice) or insolvency, we also have unilateral termination rights (i) in the event that we abandon the development and commercialization of tebipenem HBr for efficacy, safety, legal or business factors, and (ii) under certain circumstances arising out of the head license with Global Pharma.

IV Potentiator Platform Agreements

Northern License Agreement

In January 2020, we terminated our license agreement with Northern Antibiotics Oy (Ltd.) relating to SPR741. Effective January 1, 2020, the intellectual property rights associated with SPR741 have entirely reverted to Northern Antibiotics and we no longer have any rights with respect thereto and we no longer have any obligations for the cost of maintaining such intellectual property.

Cantab Agreements

In June 2016, we entered into a stock purchase agreement, or the Cantab Agreement, with Pro Bono Bio PLC, a corporation organized under the laws of England, and its affiliates, including PBB Distributions Limited, or PBB, Cantab Anti-Infectives Ltd., or CAI and New Pharma License Holdings Limited, or NPLH, in order to acquire NPLH and its intellectual property rights and assets relating to our Potentiator Platform, and our next-generation potentiating agents in particular. The intellectual property portfolio we acquired includes patents which cover SPR206 as well as other novel potentiating agents, polymyxin derivatives and other LPS or outer-membrane bacterial disrupting agents. In exchange for the acquisition of NPLH, we paid PBB upfront consideration in the amount of $0.3 million and also agreed to make milestone payments of up to $5.8 million upon the achievement of specified clinical and regulatory milestones and a payment of £5.0 million ($6.6 million as of December 31, 2019) upon the achievement of a specified commercial milestone. We also agreed to pay royalties of a low single-digit percentage based on net sales of products licensed under the agreement. In addition, Spero Cantab issued an equity interest in Spero Cantab and entered into a subscription agreement and shareholders agreement with PBB. In July 2017, we repurchased PBB's minority equity interest in Spero Cantab in exchange for a one-time nonrefundable upfront fee of approximately $0.2 million and we also amended the Cantab Agreement to increase the contingent milestone payments to PBB by an aggregate of $0.1 million. The Cantab Agreement continues indefinitely, with royalty payment obligations thereunder continuing on a product-by-product and country-by-country basis until the later of ten years after the first commercial sale of such product in such country or the expiration in such country of the last to expire valid claim of any of the applicable patents. During the three months ended December 31, 2018, we recorded $0.2 million in expense related to the achievement of regulatory milestones for SPR206.

In addition, we hold a NIAID contract that partially funds the next-generation potentiating agent development program. That contract was novated from CAI to us in December 2017. Under the contract we pay PBB a percentage of funds received from NIAID up to a maximum of $1.3 million, of which $0.3 million was paid upfront to PBB as part of this agreement. During the years ended December 31, 2019 and 2018, we recorded approximately $0.3 million and $0.4 million in expense related to amounts payable to PBB under this agreement.

Everest Medicines License Agreement

On January 4, 2019, we, through NPLH, entered into a license agreement, or the Everest License Agreement, with Everest Medicines II Limited, which Everest License Agreement also includes an option granted by our wholly owned subsidiary, Spero Potentiator, Inc., a Delaware corporation, or Potentiator. Under the terms of the Everest License Agreement, we granted Everest an exclusive license to develop, manufacture and commercialize SPR206 or products that contain SPR206, or Licensed Products, in Greater China (which includes Mainland China, Hong Kong and Macau), South Korea and certain Southeast Asian countries, collectively referred to as the Territory. We retained development, manufacturing and commercialization rights with respect to SPR206 and Licensed Products in the rest of the world and also retained the right to develop or manufacture SPR206 and Licensed Products in the Territory for use outside the Territory. In addition to the license grant to SPR206, we granted Everest a 12-month exclusive option to negotiate with us for an exclusive license to develop, manufacture and commercialize SPR741 in the Territory. For the reasons discussed above, following an evaluation of the Potentiator Platform product candidates, we determined to discontinue development of SPR741, effective January 1, 2020, and to move forward with SPR206 as our lead product candidate within the Potentiator Platform. In addition, on October 29, 2019, Everest notified us that it did not intend to exercise its option with respect to SPR741 under the Everest License Agreement. Accordingly, effective January 1, 2020, we no longer have any intellectual property rights with respect to SPR741 and we no longer have any obligations for the cost of maintaining such intellectual property.

Under the terms of the Everest License Agreement, we received an upfront payment of $3.0 million. We may also receive up to an additional $59.5 million in milestone payments upon Everest's achievement of certain developmental, regulatory and sales milestone events related to SPR206, which achievement cannot be guaranteed. We are also entitled to receive high single-digit to low double-digit royalties on net sales, if any, of Licensed Products in the Territory following regulatory approval of SPR206. Everest has the right to sublicense to affiliates and third parties in the Territory.

Everest is responsible for all costs related to developing, obtaining regulatory approval of and commercializing SPR206 and Licensed Products in the Territory, and is obligated to use commercially reasonable efforts to develop, manufacture and commercialize Licensed Products, including to achieve certain specified diligence milestones within agreed-upon periods. A joint development committee will be established between us and Everest to coordinate and review the development, manufacturing and commercialization plans with respect to Licensed Products in the Territory.

Unless earlier terminated due to certain material breaches of the contract, or otherwise, the Everest License Agreement will expire on a jurisdiction-by-jurisdiction and Licensed Product-by-Licensed Product basis until the latest to occur of expiration of the last valid claim under a licensed patent in such jurisdiction, the expiration of regulatory exclusivity in such jurisdiction or ten years after the first commercial sale of such Licensed Product in such jurisdiction. The Everest License Agreement may be terminated in its entirety by Everest upon 90 or 180 days' prior written notice, depending on the stage of development of the initial Licensed Product.

Other License and Collaboration Agreements

Gates MRI Collaboration

In June 2019, we entered into a collaboration with the Bill & Melinda Gates Medical Research Institute, or the Gates MRI, a nonprofit research institution wholly owned by the Bill and Melinda Gates Foundation, to develop SPR720 for the treatment of lung infections caused by Mycobacterium tuberculosis, or Mtb. In furtherance of the Gates MRI's charitable purposes, we also granted the Gates MRI a no cost, exclusive license to develop, manufacture and commercialize SPR720 for the treatment of tuberculosis, or TB, in low- and middle- income countries. Gates MRI will conduct and fund preclinical and clinical studies for the development of SPR720 against TB as well as certain collaborative research activities performed by us.

Vertex Assignment and License Agreement

In May 2016, we entered into an agreement with Vertex Pharmaceuticals Incorporated, or Vertex, pursuant to which Vertex assigned to us rights to patents relating to SPR720 and SPR719 (an active metabolite). The acquired patent portfolio includes protection for composition of matter, method of use, and specific key intermediates used in the manufacture of SPR719 and SPR720. We also obtained certain know-how and a license to research, develop, manufacture and sell products for a proprietary compound, as well as a transfer of materials as part of the transaction. In return, we granted Vertex an exclusive license to the assigned patents and know-how for use outside of the diagnosis, treatment or prevention of bacterial infections. In exchange for the assigned patents, we paid Vertex an upfront, one-time, non-refundable, non-creditable fee of $0.5 million, which was recognized as research and development expense, and we also agreed to pay Vertex future clinical, regulatory and commercial milestones up to $81.1 million in the aggregate and a royalty on the net sales of licensed products ranging from mid-single digits to low double digits. During the three months ended December 31, 2018, we recorded $0.2 million in expense related to the achievement of regulatory milestones for SPR720. The agreement continues in effect until the expiration of all payment obligations thereunder, with royalty payment obligations continuing on a product-by-product and country-by-country basis until the later of ten years after the first commercial sale of such product in such country or the date of expiration in such country of the last to expire applicable patent. Further, Vertex has the right to terminate the agreement if provided with notification from us of our intent to cease all development or if no material development or commercialization efforts occur for a period of 12 consecutive months.

Government Awards

As described below, through December 31, 2019, we have committed funding support of up to an aggregate of $49.7 million in non- dilutive funding from BARDA, NIAID, the DoD and CARB-X, with the potential to receive a total of up to $63.0 million (inclusive of amounts we have already received) if certain options are exercised. These awards are structured in the following manner:

- BARDA award to support the further clinical development of tebipenem HBr (previously SPR994). The BARDA award provides total reimbursement to us of $46.8 million for qualified expenses for tebipenem HBr development over a five-year period through November 2021. The award initially committed funding of $15.7 million over a three-year base period from July 2018 to June 2021 for cUTI development activities. In May 2019, the contract was modified to include additional funding of $2.5 million for tebipenem HBr, increasing the amount of initial committed funding from $15.7 million to $18.1 million. In February 2020, BARDA exercised its first option under the contract, committing $15.9 million for tebipenem HBr through November 2021. Total committed funding under the BARDA award to date is $34.1 million, including the first option exercised in 2020. There is a second option exercisable by BARDA for the remaining $12.7 million of funding, subject to specified milestones being achieved under the award agreement. As part of our tebipenem HBr collaboration with BARDA described above, there will be studies assessing the efficacy of tebipenem HBr in treatment of infections caused by biodefense threats such as anthrax, plague, and melioidosis, including a clinical trial in pneumonia patients. The Defense Threat Reduction Agency, or DTRA, will provide up to $10.0 million in addition to the total potential $46.8 million from BARDA, to cover the cost of the nonclinical biodefense aspects of the collaboration program. While such funding would be for the purpose of developing tebipenem HBr in these areas, we will not receive any funds from DTRA. Upon these achievements, BARDA may exercise its second option to fund a clinical trial in pneumonia patients to demonstrate safety and data suggestive of efficacy.
- NIAID funding for SPR206. The NIAID contract for SPR206 provides for total development funding of up to $6.5 million over a base period and three option periods. To date, funding for the base period and the first two option periods, totaling $5.9 million, have been committed. The NIAID award is subject to termination for convenience at any time by NIAID, and NIAID is not obligated to provide funding to us beyond the base period amounts from Congressionally approved annual appropriations.
- NIAID award under its Small Business Innovation Research program, or SBIR, for SPR720. This award provides up to $1.0 million of support for our SPR720 program. The scope of the program includes *in vitro* and *in vivo* assessments of SPR720 against tuberculous as well as nonclinical and manufacturing activities in support of both tuberculous and NTM indications. The NIAID SBIR award is structured as a base period followed by a single option. For the base period of March 1, 2017 through February 28, 2018, NIAID committed funding of approximately $0.6 million for the SPR720 program. In February 2018 NIAID exercised the approximately $0.4 million option, with a period of performance from March 1, 2018 through February 28, 2019. In January 2019, the period of performance for this award was extended through February 28, 2020.
- DoD funding for SPR206. In July 2019 we were awarded a $5.9 million award from the DoD Congressionally Directed Medical Research Programs (“CDMRP”) Joint Warfighter Medical Research Program, which will support, over a four-year period, the further development of SPR206. The funding will cover the costs of select Phase 1 pharmacology studies, a 28-day GLP non-human primate toxicology study, and microbiological surveillance studies that would be required for a potential NDA submission with the FDA for SPR206. This new award was preceded by a DoD cooperative agreement award made to Spero in September 2016. It was structured as a single, two-year $1.5 million award with a period of performance through September 2019. That award has now been closed out.

Intellectual Property

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover our product candidates and compositions, their methods of use and processes for their manufacture and any other inventions that are commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

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

Spero-Owned Intellectual Property Relating to tebipenem HBr and Other Compounds Under Development

We have patent applications directed to the composition of matter, formulation and/or use of tebipenem HBr, SPR741, SPR206 and SPR720 pending in the United States, Europe, Japan and other countries.

Tebipenem HBr Oral Carbapenem (Previously SPR994 – tebipenem pivoxil hydrobromide)

Our tebipenem HBr program contains one pending U.S. provisional patent application, two pending U.S. patent applications, and 20 pending foreign patent applications covering novel preparations of tebipenem pivoxil hydrobromide as of December 31, 2019, all wholly owned by us. The provisional patent application must be converted to PCT applications within one year of its May 2019 filing date. The foreign patent applications are pending in Australia, Brazil, Canada, China, Colombia, the Eurasian Patent Office, the European Patent Office, Egypt, Indonesia, Israel, India, Japan, South Korea, Mexico, New Zealand, the Philippines, Singapore, Thailand, Vietnam, and South Africa. U.S. and foreign patents covering our tebipenem pivoxil hydrobromide preparations will have statutory expiration dates of December 2037, February 2038, and May 2039. Patent term adjustments or patent term extensions could result in later expiration dates.

Next-Generation Potentiator Platform Program (Including SPR206)

The intellectual property portfolio for our next-generation polymyxin program contains patent applications and issued patents directed to composition of matter for polymyxin-like compounds with different structural features, pharmaceutical compositions comprising the same, and methods of use for these novel compounds and compositions. As of December 31, 2019, we owned one U.S. patent, two pending U.S. applications, one PCT application, three foreign patent, and 31 pending foreign patent applications in a number of jurisdictions including Argentina, Australia, Brazil, Canada, China, the European Union, Hong Kong, Israel, Japan, South Korea, Mexico, Russia, Taiwan, and Venezuela. Issued U.S. or foreign patents and any patents issuing from pending U.S. or foreign, applications covering our next-generation polymyxin program will have a statutory expiration date of May 2034, March 2035, November 2035, or June 2039. Patent term adjustments or patent term extensions could result in later expiration dates.

NTM Disease Program (SPR720)

Our intellectual property portfolio for our DNA Gyrase Inhibitor program includes issued patents and pending patent applications directed to composition of matter for SPR720, and its close analogs and prodrugs, novel solid forms of SPR720 and its prodrugs, methods of manufacture, and methods of treatment using SPR720 alone and in combination with other antibiotic compounds. All patents and patent applications in the portfolio are wholly owned by us. As of December 31, 2019, we owned eleven issued U.S. patents, 87 issued foreign patents, and 8 pending foreign patent applications. The issued and foreign patents are in a number of jurisdictions including the European Union and its member states, Argentina, Australia, Brazil, Canada, China, Hong Kong, Indonesia, Israel, India, Japan, South Korea, Mexico, New Zealand, the Philippines, Russia, Singapore, South Africa, and Taiwan. Issued U.S. and foreign patents, and patents issuing from pending U.S. and foreign applications will have statutory expiration dates of January 2032, June 2032 and July 2033. Patent term adjustments or patent term extensions could result in later expiration dates.

Patent Term and Patent Term Extensions

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug, biological product or medical device approved pursuant to a pre-market approval may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug are extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug.

Trade Secrets

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

Competition

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

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

We are developing tebipenem HBr as an oral antibiotic for use as a monotherapy for the treatment of resistant and MDR infections. If approved, tebipenem HBr would compete with several antibiotics currently in clinical development, including ceftibuten/clavulanate (“C-Scape”) from Achaogen, Inc. and sulopenem from Iterum Therapeutics Limited. We also expect that tebipenem HBr, if approved, would compete with future and current generic versions of marketed antibiotics. If approved, we believe that tebipenem HBr would compete effectively against these compounds on the basis of tebipenem HBr’s potential:

- broad range of activity against a wide variety of resistant and MDR Gram-negative bacteria;
- low probability of drug resistance;
- a favorable safety and tolerability profile supported by years of post-marketing experience in Japan;
- a convenient oral dosing regimen and opportunity to step-down from IV-administered therapy; and
- as a monotherapy treatment for MDR Gram-negative infections.

We are also developing SPR206 from our Potentiator Platform as an innovative IV-administered agent for Gram-negative infections in the hospital. If approved, SPR206 would compete with several IV-administered products marketed for the treatment of Gram-negative infections, including ceftazidime-avibactam (“Avycaz”) from Allergan plc and Pfizer Inc., ceftolozane-tazobactam (“Zerbaxa”) from Merck & Co., plazomicin (“Zemdri”) from Cipla Therapeutics, Inc., eravacycline (“Xerava”) from Tetraphase Pharmaceuticals, Inc., and meropenem-vaborbactam (“Vabomere”) from Melinta Therapeutics, Inc. There are also a number of IV-administered product candidates in late-stage clinical development that are intended to treat resistant Gram-negative infections, including cefiderocol from Shionogi & Co. Ltd., and imipenem-relebactam from Merck & Co. Each of these products and product candidates employs a mechanism of action that differs from the mechanism of action employed by SPR741.

We are developing SPR720 to be the first approved oral treatment for NTM disease. There are currently no oral agents approved to treat NTM disease. Only one drug is approved to treat NTM infection that would potentially compete with SPR720 called Arikayce from Insmed, an inhaled version of a commonly used drug in the hospital setting called amikacin. It should be noted that combination therapy is recommended for treating this condition.

Government Regulation and Product Approval

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

Recent Changes in the Regulatory Landscape

The FDA's Division of Anti-Infective Products, or DAIP, has undergone evolution in recent years, primarily driven by concerns that increasingly less effective antibiotics may have been approved in the last 10 to 15 years and a desire to bring what DAIP perceives to be greater statistical rigor to their analyses. The impact of this was a rethinking of how antibiotic efficacy is measured in clinical trials, and a review of the statistical tools used to analyze the data. In February 2015, the FDA published guidance documents for industry entitled "Complicated Urinary Tract Infections: Developing Drugs for Treatment" and guidance entitled "Complicated Intra-Abdominal Infections: Developing Drugs for Treatment." The purpose of these guidance documents is to address considerations surrounding the clinical development of drugs for cUTI and cIAI indications, including clinical trial design and efficacy. Additionally, in August 2017, the FDA published a guidance document entitled "Antibacterial Therapies for Patients With an Unmet Medical Need for the Treatment of Serious Bacterial Diseases," setting forth its current thinking with respect to development programs and clinical trial designs for antibacterial drugs to treat serious bacterial diseases.

On December 13, 2016, President Obama signed into law the Cures Act, which is intended to accelerate medical product development. Section 3042 of the Cures Act establishes the limited population pathway for certain antibacterial or antifungal drugs intended to treat targeted groups of patients suffering from serious or life-threatening infections where unmet need exists. Approvals of these limited population drugs are expected to rely on data from smaller clinical trials than would ordinarily be required by the FDA. For drugs approved through this pathway, the statement "Limited Population" will appear prominently next to the drug's name in labeling, which is intended to provide notice to healthcare providers that the drug is indicated for use in a limited and specific population of patients.

U.S. Government Regulation

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

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

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with GLP regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with GCP to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of audits of clinical trial sites conducted by FDA to assure compliance with GCPs and the integrity of clinical data; and
- payment of user fees and securing FDA review and approval of the NDA.

Preclinical Studies

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

Clinical Trials

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

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

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

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

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

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

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the nonclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision. Furthermore, the FDA is not required to complete its review within the established ten-month timeframe and may extend the review process by issuing requests for additional information or clarification.

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

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

Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

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

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

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

The FDA generally accepts data from foreign clinical trials in support of an NDA if the trials were conducted under an IND. If a foreign clinical trial is not conducted under an IND, the FDA nevertheless may accept the data in support of an NDA if the study was conducted in accordance with GCPs and the FDA is able to validate the data through an on-site inspection, if deemed necessary. Although the FDA generally requests that marketing applications be supported by some data from domestic clinical trials, the FDA may accept foreign data as the sole basis for marketing approval if (1) the foreign data are applicable to the U.S. population and U.S. medical practice, (2) the studies were performed by clinical investigators with recognized competence, and (3) the data may be considered valid without the need for an on-site inspection or, if the FDA considers the inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

The testing and approval process for an NDA requires substantial time, effort and financial resources, and each may take several years to complete. Data obtained from preclinical and clinical testing are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all.

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

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

Special FDA Expedited Review and Approval Programs

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

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need, or if the drug qualifies as a QIDP under the GAIN Act. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides additional opportunities for interaction with the FDA's review team and may allow for rolling review of NDA components before the completed application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply.

The FDA may give a priority review designation to drugs that offer major advances in treatment for a serious condition, or provide a treatment where no adequate therapy exists. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Under the current PDUFA agreement, these six and ten month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, meaning that it may be approved on (i) the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or (ii) on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Moreover, under the provisions of the Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted in 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

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

Post-Approval Requirements

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

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

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

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

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

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

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

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

Exclusivity and Approval of Competing Products

Hatch-Waxman Exclusivity

Market and data exclusivity provisions under the FDCA can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the activity of the drug substance. We believe that our product candidates are new chemical entities. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company that references the previously approved drug. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA, or supplement to an existing NDA or 505(b)(2) NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant, are deemed by the FDA to be essential to the approval of the application or supplement. Three-year exclusivity may be awarded for changes to a previously approved drug product, such as new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. For drug products that contain an “antibiotic” ingredient approved prior to 1997, the statute imposes certain limitations on the award of non-patent exclusivity. However, we do not believe these limitations would apply to tebipenem HBr or any of our other investigational antibiotics.

Qualified Infectious Disease Product Exclusivity

Under the GAIN Act provisions of FDASIA, which was signed into law in July 2012, the FDA may designate a product as a qualified infectious disease product, or QIDP. In order to receive this designation, a drug must qualify as an antibiotic or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by either (i) an antibiotic or antifungal resistant pathogen, including novel or emerging infectious pathogens, or (ii) a so-called “qualifying pathogen” found on a list of potentially dangerous, drug-resistant organisms to be established and maintained by the FDA under the new law. A sponsor must request such designation before submitting a marketing application. We obtained a QIDP designation for the oral formulation of tebipenem HBr for cUTI in November 2016 and CABP and DFI in April 2017. We were granted QIDP designation by the FDA for SPR206 in October 2018 for the treatment of cUTI and hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP). We were granted QIDP designation for SPR720 capsule for oral use for the treatment of lung infections caused by nontuberculous mycobacteria and for the treatment of lung infections caused by *Mycobacterium tuberculosis*.

Upon approving an application for a qualified infectious disease product, the FDA will extend by an additional five years any non-patent marketing exclusivity period awarded, such as a five-year exclusivity period awarded for a new molecular entity. For example, this extension is in addition to any pediatric exclusivity extension awarded.

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

Orphan Drug Designation and Exclusivity

In March 2020, the FDA granted orphan drug designation for SPR720. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for this type of disease or condition will be recovered from sales in the U.S. for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use will be disclosed publicly by the FDA; the posting will also indicate whether a drug is no longer designated as an orphan drug. More than one product candidate may receive an orphan drug designation for the same indication. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to seven years of orphan product exclusivity, except in very limited circumstances. The FDA issued a final rule intended to clarify what constitutes some of those limited circumstances. For example, the FDA will not recognize orphan drug exclusive approval if a sponsor fails to demonstrate upon approval that the drug is clinically superior to a previously approved drug, regardless of whether or not the approved drug was designated an orphan drug or had orphan drug exclusivity. Thus, orphan drug exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug as defined by the FDA and we are not able to show the clinical superiority of our drug or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. The FDA continues to periodically provide additional clarification, and in July 2018 published a final guidance entitled, "Clarification of Orphan Designation of Drugs and Biologics for Pediatric Subpopulations of Common Diseases,"

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 European Union and Australia, before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product authorization, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Before clinical trials may be conducted in any EU Member State, a sponsor must submit a clinical trial authorization application, or CTA, which must be approved in each country in which the sponsor intends to perform a clinical trial. The procedure for submitting a CTA was set forth in an existing EU Clinical Trial Directive. However, the way clinical trials are conducted in the EU will undergo a major change when the Clinical Trial Regulation becomes effective in 2019. The Regulation harmonizes the assessment and supervision processes for clinical trials throughout the EU, via an EU portal and database. The European Medicines Agency, or the EMA, will set up and maintain the portal and database, in collaboration with the Member States and the European Commission.

The goal of Clinical Trial Regulation is to create an environment that is favorable to conducting clinical trials in the EU, with the highest standards of safety for participants and increased transparency of trial information. The Regulation will require consistent rules for conducting clinical trials throughout the EU and information on the authorization, conduct and results of each clinical trial carried out in the EU to be publicly available.

When the Regulation becomes applicable, it will replace the existing EU Clinical Trial Directive and national legislation that was put in place to implement the Directive. It will also apply to trials authorized under the previous legislation if they are still ongoing three years after the Regulation becomes effective. The authorization and oversight of clinical trials will remain the responsibility of Member States, with EMA managing the database and supervising content publication on the public website.

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

Pharmaceutical Coverage and Reimbursement

Sales of our products will depend, in part, on the availability and extent of coverage and reimbursement by third-party payors, such as government health programs, including Medicare and Medicaid, commercial insurance and managed healthcare organizations. These third-party payors are increasingly challenging the price and limiting the coverage and reimbursement amounts for medical products and services.

The containment of healthcare costs has become a priority for federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor to not cover our product candidates could reduce physician usage of the product candidate and have a material adverse effect on our sales, results of operations and financial condition.

In the United States, the federal government provides health insurance for people who are 65 or older, and certain people with disabilities or certain conditions irrespective of their age, through the Medicare program, which is administered by the Centers for Medicare & Medicaid Services, or CMS. Coverage and reimbursement for products and services under Medicare are determined in accordance with the Social Security Act and pursuant to regulations promulgated by CMS, as well as the agency's coverage and reimbursement guidance and determinations. Drugs and other products that are utilized within the hospital in-patient setting are typically reimbursed under a prospective payment system, or a predetermined payment amount that is based on diagnosis related groups, or DRGs for Medicare patients and under a bundled payment for commercially insured patients. These payment amounts differ by type of diagnoses, procedures performed and the severity of the patient's condition, among other things. A drug that is used in a treatment or procedure under a specific DRG or bundled payment is generally not eligible for any separate payment. For catastrophic cases where costs greatly exceed the bundled payment amount, the hospital may be eligible for an outlier payment that is intended to cover part of the expense above the standard payment.

Medicaid is a health insurance program for low-income children, families, pregnant women, and people with disabilities that is jointly funded by the federal and state governments, but administered by the states. In general, state Medicaid programs are required to cover drugs and biologicals of manufacturers that have entered into a Medicaid Drug Rebate Agreement, although such drugs and biologicals may be subject to prior authorization or other utilization controls.

The U.S. Congress and state legislatures from time to time propose and adopt initiatives aimed at cost containment, which could impact our ability to sell our products profitably. For example, the federal Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, known collectively as the ACA, among other things, contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of general controls and measures, coupled with the tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceutical drugs. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for manufacturers' outpatient drugs furnished to Medicaid patients. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by enlarging the population potentially eligible for Medicaid drug benefits.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. Both Congress and President Trump have expressed their intention to repeal or repeal and replace the ACA, and as a result certain sections of the ACA have not been fully implemented or effectively repealed. The uncertainty around the future of the ACA, and in particular the impact to reimbursement levels, may lead to uncertainty or delay in the purchasing decisions of our customers, which may in turn negatively impact our product sales. If there are not adequate reimbursement levels, our business and results of operations could be adversely affected.

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

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

Other Healthcare Laws

Although we currently do not have any products on the market, if our product candidates are approved and we begin commercialization, we may be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Manufacturing

We do not own or operate manufacturing facilities for the production of any of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on a limited number of third-party contract manufacturers for all of our required raw materials, drug substance, and finished drug product for our preclinical research and clinical trials. We currently employ internal resources to manage our manufacturing. We intend to have two suppliers for tebipenem HBr’s active pharmaceutical ingredient. Each supplier would be capable of producing kilogram quantities for commercial scale and would be able to produce over 10kg of active pharmaceutical ingredient under cGMP conditions.

Employees

As of December 31, 2019, we had 57 full-time employees, including a total of 14 employees with M.D. or Ph.D. degrees. 37 employees were primarily engaged in research and development activities, with the rest providing administrative, business and operations support. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our employee relations to be good.

Our Corporate Information

We were formed as Spero Therapeutics, LLC in December 2013 under the laws of the State of Delaware. On June 30, 2017, through a series of transactions, Spero Therapeutics, LLC merged with and into Spero Therapeutics, Inc. (formerly known as Spero OpCo, Inc.), a Delaware corporation. Our principal executive offices are located at 675 Massachusetts Avenue, Cambridge, Massachusetts 02139, and our telephone number is (857) 242-1600. Our website address is www.sperotherapeutics.com.

Available Information

Financial and other information about us is available on our website. We make available on our website, free of charge, copies of our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the U.S. Securities and Exchange Commission, or the SEC. The information contained in our website is not intended to be a part of this filing.

Item 1A. Risk Factors.

Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report on Form 10-K, including the section of this Annual Report on Form 10-K titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes, and in other documents that we file with the SEC, in evaluating our company and our business. Investing in our common stock involves a high degree of risk. If any of the events described in the following risk factors and the risks described elsewhere in this Annual Report on Form 10-K occurs, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected and the trading price of our common stock could decline. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this Annual Report on Form 10-K.

Risks Related to Our Financial Position and Need for Additional Capital

We have not generated any revenue from the sale of our products, have a history of losses and expect to incur substantial future losses. The report of our auditor on our consolidated financial statements expresses substantial doubt about our ability to continue as a going concern; if we are unable to obtain additional capital, we may not be able to continue our operations on the scope or scale as currently conducted, and that could have a material adverse effect on our business, results of operations and financial condition.

We have not generated any revenue from the sale of our products and have incurred losses in each year since our inception in 2013. Our net losses were $60.9 million and $41.7 million during the years ended December 31, 2019 and 2018, respectively. All of our product candidates are in development, none have been approved for sale and we may never have a product candidate approved for commercialization.

In accordance with Accounting Standards Update ("ASU") 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40), we are required to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern from the issuance date of our financial statements. Based on our current plans, we believe that our existing cash, cash equivalents and marketable securities as of December 31, 2019, together with committed funding from our BARDA contract and other non-dilutive funding commitments, together with the net proceeds from our rights offering completed in early March 2020, will not be sufficient to fund our operating expenses and capital expenditure requirements, as currently planned, for more than one year. Specifically we believe these funds will enable us to fund our operating expenses and capital expenditure requirements into the first quarter of 2021, including through the filing of an NDA for tebipenem HBr. Because these funds will not sufficient to fund our operations as currently planned for more than one year beyond the filing date of this Annual Report on Form 10-K, we have determined that there is substantial doubt regarding our ability to continue as a going concern. Our consolidated financial statements as of December 31, 2019 were prepared under the assumption that we will continue as a going concern for the next twelve months. As a result, the opinion from our independent registered public accounting firm with respect to our annual financial statements contains an explanatory paragraph about such substantial doubt about our ability to continue as a going concern. Our ability to continue as a going concern is dependent upon our ability to obtain additional equity or debt financing, attain further operating efficiencies, reduce expenditures, and, ultimately, to generate revenue. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. The substantial doubt about our ability to continue as a going concern may adversely affect our stock price and our ability to raise capital. There is no assurance that we will be successful in obtaining sufficient funding on acceptable terms, if at all, and we could be forced to delay, reduce or eliminate some or all of our research and development programs, product portfolio expansion or commercialization efforts, which could materially adversely affect our business prospects or our ability to continue operations.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future; if we are unable to achieve commercialization, revenue from product sales, and, ultimately, profitability, the market value of our common stock will likely decline.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future as we continue to advance our product candidates through preclinical and clinical development and seek marketing approval for such candidates if clinical trials are successful. Our expenses will also increase substantially if and as we:

- conduct additional clinical trials and studies of our product candidates;
- continue to discover and develop additional product candidates;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of any product candidates for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, scientific and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- acquire or in-license other product candidates and technologies.

If our product candidates fail to demonstrate safety and efficacy in clinical trials, do not gain regulatory approval, or do not achieve market acceptance following regulatory approval and commercialization, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. If we are unable to achieve and sustain profitability, the market value of our common stock will likely decline.

Because of the numerous risks and uncertainties associated with developing biopharmaceutical products, we are unable to predict the extent of any future losses or when, if ever, we will become profitable. Our expenses could increase if we are required by the FDA, or any comparable foreign regulatory authority to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates.

We expect that we will need substantial additional funding. If we are unable to raise capital when needed, or do not receive payment under our government awards, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete. We expect that our expenses will increase substantially as we commence and advance our ongoing and planned clinical trials and other studies of tebipenem HBr, SPR720 and SPR206, seek marketing approval for tebipenem HBr if clinical trials are successful, and evaluate the advancement of our other product candidates. If we obtain marketing approval for tebipenem HBr or any other product candidate, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Some of these expenses may be incurred in advance of marketing approval, and could be substantial. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations, licensing arrangements, government funding or other sources. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to pursue our business strategy.

We believe that our existing cash, cash equivalents and marketable securities as of December 31, 2019, together with committed funding from our BARDA contract and other non-dilutive funding commitments, together with the net proceeds from our rights offering completed in early March 2020, will enable us to fund our operating expenses and capital expenditure requirements into the first quarter of 2021, including through the filing of an NDA for tebipenem HBr. Our cash forecasts are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the timing, costs and results of our ongoing and planned clinical trials of tebipenem HBr;
- the timing, costs and results of our ongoing, planned and potential clinical trials for other product candidates;
- the amount of funding that we receive under our government awards;

- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for tebipenem HBr and other product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the receipt of marketing approval and revenue received from any potential commercial sales of tebipenem HBr;
- the terms and timing of any future collaborations, licensing or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to our license agreements;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;
- the costs of our continued operation as a public company; and
- the extent to which we in-license or acquire other products and technologies.

As of December 31, 2019, our non-dilutive sources of funding consisted of an award from BARDA for tebipenem HBr, an award from NIAID under its Small Business Innovation Research program or SBIR, for our SPR720 program, an award from NIAID for SPR206, awards from CARB-X and the DoD that provide partial funding for the development of our Potentiator Platform product candidates and an award from the DoD Congressionally Directed Medical Research Programs ("CDMRP") Joint Warfighter Medical Research Program for SPR206.

The BARDA award provides total reimbursement to us of $46.8 million for qualified expenses for tebipenem HBr development over a five-year period through November 2021. The award initially committed funding of $15.7 million over a three-year base period from July 2018 to June 2021 for cUTI development activities. In May 2019, the contract was modified to include additional funding of $2.5 million for tebipenem HBr, increasing the amount of initial committed funding from $15.7 million to $18.1 million. In February 2020, BARDA exercised its first option under the contract, committing $15.9 million for tebipenem HBr through November 2021. Total committed funding under the BARDA award to date is $34.1 million, including the first option exercised in 2020. There is a second option exercisable by BARDA for the remaining $12.7 million of funding, subject to specified milestones being achieved under the award agreement. As part of our tebipenem HBr collaboration with BARDA described above, there will be studies assessing the efficacy of tebipenem HBr in treatment of infections caused by biodefense threats such as anthrax, plague, and melioidosis, including a clinical trial in pneumonia patients. The Defense Threat Reduction Agency, or DTRA, will provide up to $10.0 million in addition to the total potential $46.8 million from BARDA, to cover the cost of the nonclinical biodefense aspects of the collaboration program. While such funding would be for the purpose of developing tebipenem HBr in these areas, we will not receive any funds from DTRA. Upon these achievements, BARDA may exercise its second option to fund a bronchoalveolar lavage study to demonstrate safety and lung exposure sufficient to support a clinical trial in pneumonia patients to demonstrate safety and data suggestive of efficacy.

The NIAID contract for SPR206 provides for total development funding of up to $6.5 million over a base period and three option periods. To date, funding for the base period and the first two option periods totaling $5.9 million have been committed. The NIAID SBIR award is structured as a base period followed by a single option. For the base period of March 1, 2017 through February 28, 2018, NIAID committed funding of approximately $0.6 million for the SPR720 program. In February 2018 NIAID exercised the approximately $0.4 million option, which had an initial a period of performance from March 1, 2018 through February 28, 2019. In January 2019, the period of performance for this award was extended for an additional 12-month period. Our DoD cooperative agreement is structured as a single, two-year $1.5 million award. We are eligible for the full funding from the DoD and there are no options to be exercised at a later date. The CARB-X award is structured as a base period followed by two sequential options. In March 2017, CARB-X committed funds of $1.5 million to support SPR741 development efforts for the period from April 1, 2017 to March 31, 2018. On March 12, 2018, CARB-X committed an additional $0.4 million related to the first option for a period from December 1, 2017 to March 31, 2018. There will be no additional options exercised under the CARB-X award. The NIAID award is subject to termination for convenience at any time by NIAID. NIAID is not obligated to provide funding to us beyond the base period amounts from Congressionally approved annual appropriations. The DoD CDMRP award commits funding of $5.9 million over a four-year period to cover the costs of select Phase 1 pharmacology studies, 28-day GLP non-human primate toxicology study and microbiological surveillance studies that would be required for a potential NDA submission with the FDA for SPR206.

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

Unless and until we can generate a substantial amount of revenue from our product candidates, we expect to finance our future cash needs through public or private equity offerings, debt financings, collaborations, licensing arrangements and government funding arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. We filed a universal shelf registration statement on Form S-3 (Registration No. 333-228661) with the SEC, which was declared effective on December 11, 2018 and pursuant to which we registered for sale up to $200.0 million of any combination of our common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that we may determine, including up to $50.0 million of our common stock available for issuance pursuant to an at-the-market offering program sales agreement that we entered into with Cantor Fitzgerald & Co., or Cantor. Under the sales agreement, Cantor may sell shares of our common stock by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415 of the Securities Act, subject to the terms of the sales agreement.

On June 12, 2019, we entered into a securities purchase agreement with Novo Holdings A/S ("Novo") to sell up to an aggregate of $10.0 million of our common stock in two closings pursuant to our effective registration statement on Form S-3 (Registration No. 333-228661). The initial closing occurred on June 14, 2019 and consisted of 465,983 shares of common stock sold at a price of $10.73 per share for gross proceeds of approximately $5.0 million, prior to deducting offering expenses. The second closing occurred on October 18, 2019 and consisted of 465,116 shares of common stock sold at a price of $10.75 per share for gross proceeds of approximately $5.0 million, prior to deducting offering expenses.

We may seek to raise additional capital at any time. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, the ownership interest of our then existing stockholders may be materially diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect the rights of our stockholders. In addition, debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, which could adversely affect our ability to conduct our business. In addition, securing additional financing would require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us.

Our ability to use our net operating loss carryforwards may be limited.

As of December 31, 2019, we had U.S. federal, state and foreign net operating loss carryforwards, or NOLs, of $156.8 million, $157.8 million and $7.7 million, respectively. The federal NOLs of $73.0 million will expire at various dates from 2033 to 2037 and approximately $83.8 million can be carried forward indefinitely. The state NOLs begin to expire in 2033 and will expire at various dates through 2039. The foreign NOLs do not expire. Utilization of these NOLs depends on many factors, including our future income, which cannot be assured. These NOLs could expire unused and be unavailable to offset our future income tax liabilities. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership by 5% 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 income may be limited. We have not determined if we have experienced Section 382 ownership changes in the past and if a portion of our NOLs is subject to an annual limitation under Section 382. In addition, we may experience ownership changes in the future as a result of subsequent changes in our stock ownership, some of which may be outside of our control. If we determine that an ownership change has occurred and our ability to use our historical NOLs is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

Under recently enacted U.S. federal tax legislation, although the treatment of net operating loss carryforwards arising in tax years beginning on or before December 31, 2017 has generally not changed, net operating loss carryforwards arising in tax years beginning after December 31, 2017 may be used to offset only 80% of taxable income. In addition, net operating losses arising in tax years beginning after December 31, 2017 may be carried forward indefinitely, as opposed to the 20-year carryforward under prior law.

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

We were established in 2013 and began operations in 2014. Our operations to date have been limited to financing and staffing our company, developing our technology and developing tebipenem HBr and our other product candidates. We have not yet demonstrated an ability to successfully complete a large-scale, pivotal clinical trial, obtain marketing approval, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will eventually need to transition from a company with a 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, stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Risks Related to Product Development and Commercialization

We are heavily dependent on the success of tebipenem HBr, which is still under development, and our ability to develop, obtain marketing approval for and successfully commercialize tebipenem HBr. If we are unable to develop, obtain marketing approval for and successfully commercialize tebipenem HBr, or if we experience significant delays in doing so, our business could be materially harmed.

We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of tebipenem HBr as a product candidate for the treatment of MDR bacterial infections. Our near-term prospects are substantially dependent on our ability to develop, obtain marketing approval for and successfully commercialize tebipenem HBr. The success of tebipenem HBr will depend on several factors, including the following:

- successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers to obtain manufacturing supply in compliance with all regulatory requirements;
- obtainment and maintenance of patent, trade secret protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain our license agreement with Meiji with respect to tebipenem HBr;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales of tebipenem HBr, if approved, whether alone or in collaboration with others;
- acceptance of tebipenem HBr, if approved, by patients, the relevant medical communities and third-party payors;
- competition with other therapies;
- establishment and maintenance of adequate health care coverage and reimbursement;
- continued compliance with any post-marketing requirements imposed by applicable regulatory authorities, including any required post-marketing clinical trials or the elements of any post-marketing Risk Evaluation and Mitigation Strategy, or REMS, that may be required by the FDA or comparable requirements in other jurisdictions to ensure the benefits of tebipenem HBr outweigh its risks; and
- a continued acceptable safety profile of tebipenem HBr following approval.

Successful development of tebipenem HBr for any additional indications would be subject to these same risks.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to develop, receive marketing approval for, or successfully commercialize tebipenem HBr, or if we experience delays as a result of any of these factors or otherwise, our business could be materially harmed. Even if we successfully obtain regulatory approvals to manufacture and market tebipenem HBr, our revenues will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets for patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such product, if approved.

We have no experience as a company in obtaining regulatory approval for a drug.

As a company, we have never obtained regulatory approval for, or commercialized, a drug. It is possible that the FDA may refuse to accept any or all of our planned new drug applications, or NDAs, for substantive review or may conclude after review of our data that our application is insufficient to obtain regulatory approval for any current or future product candidates. If the FDA does not approve any of our planned NDAs, it may require that we conduct additional costly clinical, nonclinical or manufacturing validation studies before it will reconsider our applications. Depending on the extent of these or any other FDA-required studies, approval of any NDA or other application that we submit may be significantly delayed, possibly for several years, or may require us to expend more resources than we have available. Any failure or delay in obtaining regulatory approvals would prevent us from commercializing tebipenem HBr or any of our other product candidates for which we may seek regulatory approval, generating revenues and achieving and sustaining profitability. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve any NDA or other application that we submit. If any of these outcomes occur, we may be forced to abandon the development of our product candidates, which would materially adversely affect our business and could potentially cause us to cease operations. We face similar risks for our applications in foreign jurisdictions.

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

We may not commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA or in other countries without obtaining approvals from comparable foreign regulatory authorities, such as the European Medicines Agency, or EMA, and we may never receive such approvals. We must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We have not previously submitted an NDA to the FDA or similar applications to comparable foreign regulatory authorities for any of our product candidates.

The clinical development of tebipenem HBr and any of our other product candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to demonstrate efficacy in a trial or across a broad population of patients, the occurrence of severe adverse events, failure to comply with protocols or applicable regulatory requirements, and determination by the FDA or any comparable foreign regulatory authority that a drug product is not approvable. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in clinical trials, even after promising results in earlier nonclinical studies or clinical trials. The results of preclinical and other nonclinical studies and/or early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Notwithstanding any promising results in early nonclinical studies or clinical trials, we cannot be certain that we will not face similar setbacks. For example, although tebipenem HBr is a new formulation of the active pharmaceutical ingredient tebipenem that exhibited a favorable safety and efficacy profile during clinical trials conducted by Meiji and a global pharmaceutical company, which we refer to as Global Pharma, in Japan, we may nonetheless fail to achieve success in our clinical trials. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates.

In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we believe that the results of our clinical trials warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

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

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

- the FDA or other comparable foreign regulatory authorities may disagree as to the design or implementation of our clinical trials;
- we may be delayed in or fail to reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- 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 clinical trials;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the FDA 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;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical trials of our product candidates for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we enter into 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; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the institutional review boards, or IRBs, of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, if any, for such trial or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug or changes in governmental regulations or administrative actions.

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

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

Our failure to successfully initiate and complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business. Our product candidate development costs will also increase if we experience delays in testing or marketing approvals and we may be required to obtain additional funds to complete clinical trials. We cannot make assurances that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our trials after they have begun. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of tebipenem HBr or any other product candidate.

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

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

- the size and nature of the target patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the patient eligibility criteria for participation in the clinical trial;
- the design of the clinical trial;
- our ability to recruit clinical trial investigators with appropriate competencies and experience;
- competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications that we are investigating;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

The inclusion and exclusion criteria for our ongoing Phase 3 clinical trial of tebipenem HBr may adversely affect our enrollment rates for patients in these trials. In addition, many of our competitors also have ongoing clinical trials for product candidates that would treat the same indications as we contemplate for tebipenem HBr or our other product candidates, and patients who would otherwise be eligible for any clinical trials we may conduct for such product candidates may instead enroll in clinical trials of our competitors' product candidates.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or might require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, slow down or halt our product candidate development and approval process and jeopardize our ability to seek and obtain the marketing approval required to commence product sales and generate revenue, which would cause the value of our company to decline and limit our ability to obtain additional financing if needed.

Our clinical program for tebipenem HBr is subject to a number of specific risks that may affect the outcome of the trial, including the use of a new formulation of the active pharmaceutical ingredient, tebipenem.

Our pivotal Phase 3 clinical trial of tebipenem HBr is subject to a number of specific risks arising from our clinical program and the design of the trial. We have not conducted a clinical trial of tebipenem HBr in patients with cUTI, who will be the subjects of the clinical trial, and we have no direct clinical evidence that tebipenem HBr is effective in treating cUTIs in humans. Although we believe that tebipenem HBr has the potential to treat cUTI in humans based on the results of our nonclinical *in vitro* and *in vivo* animal model studies, together with Meiji's and Global Pharma's Phase 2 clinical trial results, these results are not necessarily predictive of the results of our planned clinical trials and we cannot guarantee that tebipenem HBr will demonstrate the expected efficacy in our pivotal Phase 3 clinical trial patients. We also cannot guarantee that the projections made from the pharmacokinetic and pharmacodynamic models that we developed from our nonclinical and clinical tebipenem HBr studies will be validated in our pivotal Phase 3 clinical trial.

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

To support our accelerated clinical development strategy for tebipenem HBr, we are relying, in part, on clinical data from two exploratory Phase 2 clinical trials conducted by Meiji (ME1211) and Global Pharma (L-084 04) in Japan, which were not conducted in accordance with FDA guidance for clinical trials in patients with cUTI. To the extent that these clinical trial design differences limit our use of the clinical data, our proposed clinical trial plan for tebipenem HBr with the FDA could be materially delayed and we may incur material additional costs.

There are significant differences in the trial design for the two exploratory Phase 2 clinical trials conducted by Meiji and its partner in Japan compared to the clinical trial design described by the FDA in its guidance for clinical trials in patients with cUTI, including:

- The studies were not randomized and were open-label and had no comparator arm. Treatment assignments were made by the investigators;
- The inclusion criteria specified complicated UTI as an entry criterion, but other than retained residual volume (100 ml) there were no other criteria defining “complicated” UTI;
- While L-084 04 excluded patients who received prior antibiotics and who had no clinical response, there were no parameters or limits for inclusion (e.g., less than 24 hours of a potentially effective antibiotic or number of doses). ME1211 did not specifically mention prior antibiotic use;
- While urine cultures were obtained at baseline, these were not quantitative, and there was no minimum requirement for bacterial load for entry;
- While microbiological outcome was assessed, the definitions did not include a minimum reduction in bacterial counts (i.e., a reduction to less than 10^4 cfu/ml);
- Clinical outcomes were global assessments by the investigators and did not specifically mention the resolution of baseline signs and symptoms; and
- The primary endpoint was not a composite of both clinical and microbiological outcomes.

If our pivotal Phase 3 clinical trial of tebipenem HBr does not yield data that confirm the clinical and microbiological efficacy of tebipenem HBr as suggested by the results from the Phase 2 clinical trials conducted by Meiji and its partner, then our clinical pathway for tebipenem HBr could be delayed and our business could be materially harmed.

Preliminary or interim data from our clinical studies that we announce or publish from time to time, including preliminary data from our Phase 1 clinical trial of tebipenem HBr and our dose-selection findings, 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.

We currently have no products approved for sale and we cannot guarantee that we will ever have marketable products. Clinical failure can occur at any stage of clinical development. Clinical trials may produce negative or inconclusive results, and we or any future collaborators may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective for use in a diverse population before we can seek marketing approvals for their commercial sale. Success in preclinical studies and early-stage clinical trials does not mean that future larger registration clinical trials will be successful. This is because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and comparable foreign regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials.

Preliminary or interim data from our clinical studies are not necessarily predictive of final data. Preliminary and interim data are subject to the risk that one or more of the clinical outcomes may materially change, as more patient data become available and we issue our final clinical study report. Preliminary or interim 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. Adverse differences between preliminary or interim data and final data could affect our planned clinical path for tebipenem HBr, including potentially increasing cost and/or causing delay in such development.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We therefore do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain marketing approval to market our product candidates.

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

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

While the active pharmaceutical ingredient in tebipenem HBr, tebipenem, is approved in Japan, our formulation of tebipenem, tebipenem HBr, has not yet been tested in patients. There may be unforeseen serious adverse events or side effects that differ from those seen in the Japanese studies. To date, patients treated with the active ingredient in tebipenem HBr have experienced drug-related side effects including diarrhea, temporary increases in hepatic enzymes, allergic reactions, rashes and convulsions. To date, tebipenem HBr has generally been well tolerated in clinical trials conducted in healthy subjects and there have been no reports of serious adverse events related to tebipenem HBr, but additional adverse events may emerge in any subsequent clinical trials.

If unexpected adverse events occur in any of our ongoing or planned clinical trials, we may need to abandon development of our product candidates, or limit development to lower doses or to certain uses or subpopulations in which the undesirable side effects or other unfavorable characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing are later found to cause undesirable or unexpected side effects that prevented further development of the compound.

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

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

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

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

Even if we obtain FDA or other regulatory approvals and are able to launch tebipenem HBr or any other product candidate commercially, the approved product candidate may nonetheless fail to gain sufficient market acceptance among physicians, patients, hospitals (including pharmacy directors) and third-party payors and, ultimately, may not be commercially successful. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of coverage and reimbursement for existing therapies. If an approved product candidate does not achieve an adequate level of acceptance, we may not generate significant product revenues or any profits from operations. The degree of market acceptance of any product candidate for which we receive approval depends on a number of factors, including:

- the efficacy and safety of the product candidate as demonstrated in clinical trials;
- relative convenience and ease of administration;
- the clinical indications for which the product candidate is approved;
- the potential and perceived advantages and disadvantages of the product candidates, including cost and clinical benefit relative to alternative treatments;
- the willingness of physicians to prescribe the product and of the target patient population to try new therapies;
- the willingness of hospital pharmacy directors to purchase the product for their formularies;
- acceptance by physicians, patients, operators of hospitals and treatment facilities and parties responsible for coverage and reimbursement of the product;
- the availability of coverage and adequate reimbursement by third-party payors and government authorities;
- the effectiveness of our sales and marketing efforts;
- the strength of marketing and distribution support;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling or an approved risk evaluation and mitigation strategy;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular infections;
- the approval of other new products for the same indications;
- the timing of market introduction of the approved product as well as competitive products;
- adverse publicity about the product or favorable publicity about competitive products;
- the emergence of bacterial resistance to the product; and
- the rate at which resistance to other drugs in the target infections grows.

Any failure by tebipenem HBr or any other product candidate that obtains regulatory approval to achieve market acceptance or commercial success would adversely affect our business prospects.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential.

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

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

We do not have a sales, marketing or distribution infrastructure and we have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource those functions to third parties. We intend to build a commercial organization in the United States 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. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we intend to target. If we are unable to establish a sales force and marketing and distribution capabilities, our operating results may be adversely affected.

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

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to 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 relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

We intend to use collaborators to assist with the commercialization of tebipenem HBr and any other product candidate outside the United States. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us would likely be lower than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we likely would have little control over such third parties, and any of them might fail to devote the necessary resources and attention to sell and market our products effectively.

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

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

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

There are a variety of available oral therapies marketed for the treatment urinary tract infections that we would expect would compete with tebipenem HBr, such as Levaquin, Cipro and Bactrim. Many of the available therapies are well established and widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products, for example in the fluoroquinolone class. However, the susceptibility of urinary tract pathogens to the existing treatment alternatives is waning. If tebipenem HBr is approved, the pricing may be at a significant premium over other competitive products. This may make it difficult for tebipenem HBr to compete with these products.

There are also a number of oral product candidates in clinical development by third parties that are intended to treat UTIs. Some mid- to late-stage product candidates include ceftibuten/clavulanate (C-Scape) from Achaogen, Inc., sulopenem from Iterum Therapeutics Limited and omadacycline from Paratek Pharmaceuticals, Inc. If our competitors obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than us, it could result in our competitors establishing a strong market position before we are able to enter the market.

There are several IV-administered products marketed for the treatment of infections resistant to first-line therapy for Gram-negative infections, including ceftazidime-avibactam (Avycaz) from Allergan plc and Pfizer Inc., ceftolozane-tazobactam (Zerbaxa) from Merck & Co., plazomicin (Zemdri) from Achaogen, Inc., eravacycline (Xerava) from Tetraphase Pharmaceuticals, Inc. and meropenem-vaborbactam (Vabomere) from Melinta Therapeutics, Inc. There are also a number of IV-administered product candidates in late-stage clinical development that are intended to treat resistant Gram-negative infections, including cefiderocol from Shionogi & Co. Ltd. and imipenem-relebactam from Merck & Co.

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

In July 2012, the Food and Drug Administration Safety and Innovation Act was passed, which included the Generating Antibiotics Incentives Now Act, or the GAIN Act. The GAIN Act is intended to provide incentives for the development of new, qualified infectious disease products. In December 2016, the Cures Act was passed, providing additional support for the development of new infectious disease products. These incentives may result in more competition in the market for new antibiotics, and may cause pharmaceutical and biotechnology companies with more resources than we have to shift their efforts towards the development of product candidates that could be competitive with tebipenem HBr and our other product candidates.

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

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

We currently expect that some of our product candidates, if approved, will be administered in a hospital inpatient setting. In the United States, governmental and other third-party payors generally reimburse hospitals a single bundled payment established on a prospective basis intended to cover all items and services provided to the patient during a single hospitalization. Hospitals bill third-party payors for all or a portion of the fees associated with the patient's hospitalization and bill patients for any deductibles or co-payments. Because there is typically no separate reimbursement for drugs administered in a hospital inpatient setting, some of our target customers may be unwilling to adopt our product candidates in light of the additional associated cost. If we are forced to lower the price we charge for our product candidates, if approved, our gross margins may decrease, which would adversely affect our ability to invest in and grow our business.

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

Increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We cannot be sure that coverage will be available for tebipenem HBr or any other product candidate that we commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for outpatient drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any approved products used on an outpatient basis that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

We cannot predict whether bacteria may develop resistance to tebipenem HBr or our other product candidates, which could affect their revenue potential.

We are developing tebipenem HBr and certain of our other product candidates to treat drug-resistant bacterial infections. The bacteria responsible for these infections evolve quickly and readily transfer their resistance mechanisms within and between species. We cannot predict whether or when bacterial resistance to tebipenem HBr or any of such other product candidates may develop.

As a carbapenem, tebipenem HBr is not active against organisms expressing a resistance mechanism mediated by enzymes known as carbapenemases. Although occurrence of this resistance mechanism is currently rare, we cannot predict whether carbapenemase-mediated resistance will become widespread in regions where we intend to market tebipenem HBr if it is approved. The growth of drug resistant infections in community settings or in countries with poor public health infrastructures, or the potential use of tebipenem HBr or any of our other product candidates outside of controlled hospital settings, could contribute to the rise of resistance. If resistance to tebipenem HBr or any of our other product candidates becomes prevalent, our ability to generate revenue from tebipenem HBr or such product candidates could suffer.

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 efforts will focus on our ongoing and planned clinical trials and potential approval of our lead product candidate, tebipenem HBr, SPR720 and our Potentiator Platform product candidate, SPR206, a key element of our strategy is to discover, develop and commercialize a portfolio of therapeutics to treat drug resistant bacterial infections. We are seeking to do so through our internal research programs and are exploring, and intend to explore in the future, strategic partnerships for the development of new product candidates.

Research programs to identify 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;
- we may be unable to successfully modify candidate compounds to be active in Gram-negative bacteria or defeat bacterial resistance mechanisms or identify viable product candidates in our screening campaigns;
- competitors may develop alternatives that render our product candidates obsolete;
- product candidates that 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; and
- the development of bacterial resistance to potential product candidates may render them ineffective against target infections.

If we are unsuccessful in identifying and developing additional product candidates, our potential for growth may be impaired.

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

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we obtain marketing approval for and commercially sell tebipenem HBr or any other product candidate. For example, we may be sued if any product that we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- reduced resources for our management to pursue our business strategy;
- decreased demand for our 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 resulting litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

Although we maintain general liability insurance and clinical trial liability insurance, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if and when we receive marketing approval for and begin selling tebipenem HBr or any other product candidate. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could adversely affect our business, financial condition, results of operations and prospects.

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 have a material adverse effect on 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. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and wastes, we cannot completely eliminate the risk of contamination or injury resulting 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.

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

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Our internal computer systems, or those of our contract research organizations or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs, and could subject us to liability.

We utilize information technology systems and networks to process, transmit and store electronic information in connection with our business activities. As the use of digital technologies has increased, cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. These threats pose a risk to the security of our systems and networks and the confidentiality, availability and integrity of our data. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects.

Despite the implementation of security measures, our internal computer systems and those of our contract research organizations and other contractors and consultants are vulnerable to damage or disruption from hacking, computer viruses, software bugs, unauthorized access, natural disasters, terrorism, war, and telecommunication, equipment and electrical failures. While we have not, to our knowledge, experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations or the operations of those third parties with which we contract, it could result in a material disruption of our programs and our business operations. For example, the loss of clinical trial data from completed or ongoing clinical trials for any of our product candidates could result in delays in our development and regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure or theft of confidential or proprietary information, we could incur liability, the further development of our product candidates could be delayed or our competitive position could be compromised.

Any such disruption or security breach, as well as any action by us or our employees or contractors that might be inconsistent with the rapidly evolving data privacy and security laws and regulations applicable within the United States and elsewhere where we conduct business, could result in enforcement actions by U.S. states, the U.S. Federal government or foreign governments, liability or sanctions under data privacy laws that protect personally identifiable information, regulatory penalties, other legal proceedings such as but not limited to private litigation, the incurrence of significant remediation costs, disruptions to our development programs, business operations and collaborations, diversion of management efforts and damage to our reputation, which could harm our business and operations. Because of the rapidly moving nature of technology and the increasing sophistication of cybersecurity threats, our measures to prevent, respond to and minimize such risks may be unsuccessful.

In addition, the European Parliament and the Council of the European Union adopted a comprehensive general data privacy regulation, or GDPR, in 2016 to replace the current European Union Data Protection Directive and related country-specific legislation. The GDPR took effect in May 2018 and governs the collection and use of personal data in the European Union. The GDPR, which is wide-ranging in scope, will impose several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, the security and confidentiality of the personal data, data breach notification and the use of third party processors in connection with the processing of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the United States, enhances enforcement authority and imposes large penalties for noncompliance, including the potential for fines of up to €20 million or 4% of the annual global revenues of the infringer, whichever is greater.

The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR has been and will continue to be a rigorous and time-intensive process that has increased and will continue to increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we or our collaborators may be subject to fines and penalties, litigation and reputational harm in connection with any European activities, which could adversely affect our business, prospects, financial condition and results of operations.

In addition, in June 2018, California enacted the California Consumer Privacy Act, or CCPA, which takes effect on January 1, 2020. The CCPA gives California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that may increase data breach litigation. Although the CCPA includes exemptions for certain clinical trials data, and HIPAA protected health information, the law may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. The CCPA has prompted a number of proposals for new federal and state privacy legislation that, if passed, could increase our potential liability, increase our compliance costs and adversely affect our business.

We or third parties upon whom we depend may be adversely affected by natural disasters and/or health epidemics, and our business, financial condition and results of operations could be adversely affected.

Natural disasters could severely disrupt our operations and have a material adverse effect on our business operations. If a natural disaster, health epidemic, or other event beyond our control occurred that prevented us from using all or a significant portion of our office and/or lab spaces, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult for us to continue our business for a substantial period of time. In December 2019, a novel strain of coronavirus was reported to have surfaced in Wuhan, China. In January 2020, this coronavirus spread to other parts of the world, including the United States and Europe, and efforts to contain the spread of this coronavirus intensified. In January 2020, the World Health Organization declared the Coronavirus outbreak a "public health emergency of international concern." The extent to which the coronavirus impacts our results will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity of the coronavirus and the actions to contain the coronavirus or treat its impact, among others.

Should the coronavirus continue to spread in the United States and Europe, our business operations could be delayed or interrupted. For instance, our clinical trials may suffer from lower than anticipated patient registration or enrollment and we may be forced to temporarily delay or pause ongoing trials. Further, if the spread of the coronavirus continues and our operations are impacted, we risk a delay, default and/or nonperformance under our existing agreements arising from force majeure. If either any of the foregoing were to occur, it could materially adversely affect our financial condition.

Risks Related to Our Dependence on Third Parties

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

Although we expect to commercialize tebipenem HBr ourselves in the United States, we intend to commercialize it outside the United States through collaboration arrangements. In addition, we may seek third-party collaborators for development and commercialization of certain of our product candidates. For instance, in January 2019, we entered into a license agreement with Everest Medicines II Limited whereby we granted Everest an exclusive license to develop, manufacture and commercialize SPR206, or products containing SPR206, in Greater China, South Korea and certain Southeast Asian countries. Additionally, in June 2019, we entered into a collaboration agreement with the Bill and Melinda Gates Medical Research Institute (the "Gates MRI") to develop SPR720 for the treatment of lung infections caused by Mycobacterium tuberculosis. Our likely collaborators for any other marketing, distribution, development, licensing or broader collaboration arrangements we may pursue include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

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

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

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

- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

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

We may have to alter our development and commercialization plans if we are not able to establish collaborations.

We will require additional funds to complete the development and potential commercialization of tebipenem HBr and our other product candidates. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. Moreover, we intend to utilize a variety of types of collaboration arrangements for the potential commercialization of our product candidates outside the United States. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include:

- the design or results of clinical trials;
- the likelihood of approval by the FDA or comparable foreign regulatory authorities;
- the potential market for the subject product candidate;
- the costs and complexities of manufacturing and delivering such product candidate to patients;
- the potential for competing products;
- our patent position protecting the product candidate, including any uncertainty with respect to our ownership of our technology or our licensor's ownership of technology we license from them, which can exist if there is a challenge to such ownership without regard to the merits of the challenge;
- the need to seek licenses or sub-licenses to third-party intellectual property; and
- industry and market conditions generally.

The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market and our business may be materially and adversely affected.

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

We do not independently conduct nonclinical studies that comply with GLP requirements. We also do not have the ability to independently conduct clinical trials of any of our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials of tebipenem HBr or our other product candidates and expect to rely on these third parties to conduct clinical trials of our other product candidates and potential product candidates. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities and increase our costs.

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

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

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

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

We do not currently have nor do we plan to build the internal infrastructure or capability to manufacture tebipenem HBr or our other product candidates for use in the conduct of our preclinical research, our clinical trials or for commercial supply. We currently rely on and expect to continue to rely on third-party contract manufacturers to manufacture supplies of tebipenem HBr and our other product candidates, and we expect to rely on third-party contract manufacturers to manufacture commercial quantities of any product candidate that we commercialize following approval for marketing by applicable regulatory authorities, if any. Reliance on third-party manufacturers entails risks, including:

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

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

If any of our product candidates are approved by any regulatory agency, we intend to enter into agreements with third-party contract manufacturers for the commercial production of those products. This process is difficult and time consuming and we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under cGMPs that are capable of manufacturing our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization.

Third-party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the United States. Facilities used by our third-party manufacturers must be approved by the FDA after we submit an NDA and before potential approval of the product candidate. Similar regulations apply to manufacturers of our product candidates for use or sale in foreign countries. We do not control the manufacturing process and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of our product candidates. The inability or failure of our manufacturers to successfully manufacture material that conforms to the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, may require us to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate. In addition, our manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and have a material adverse effect on our business, financial condition and results of operations.

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

If we fail to comply with our obligations in the agreements under which we in-license or acquire development or commercialization rights to products, technology or data from third parties, including those for tebipenem HBr, we could lose such rights that are important to our business.

We are a party to agreements with Meiji for tebipenem HBr, Vertex Pharmaceuticals for SPR720 and PBB Distributions Limited for SPR206, and we may enter into additional agreements, including license agreements, with other parties in the future that impose diligence, development and commercialization timelines, milestone payments, royalties, insurance and other obligations on us.

For example, we have an exclusive know-how license with Meiji, or the Meiji License, that gives us rights outside of specified countries in Asia to develop, manufacture, and commercialize tebipenem HBr as well as the right to use, cross-reference, file or incorporate by reference any information and relevant Meiji regulatory documentation to support any regulatory filings outside of Asia. In addition, we have the right to develop, manufacture and have manufactured tebipenem HBr in Asia solely for the purpose of furthering development, manufacturing and commercialization of tebipenem HBr outside of Asia. In exchange for those rights, we are obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop and commercialize tebipenem HBr and to implement a specified development plan, meeting specified development milestones and providing an update on progress on an annual basis. The Meiji License requires us to pay milestone payments of up to $3.0 million upon the achievement of specified clinical and regulatory milestones and royalties of a low single-digit percentage on net sales on a country-by-country basis.

If we fail to comply with our obligations to Meiji or any of our other partners, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product candidate that is covered by these agreements, which could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

Risks Related to Our U.S. Government Contracts and to Certain Grant Agreements

Our use of government funding for certain of our programs adds complexity to our research and commercialization efforts with respect to those programs and may impose requirements that increase the costs of commercialization and production of product candidates developed under those government-funded programs.

We have received significant non-dilutive financing from various government agencies for the further development of our product candidates. Such funding sources may pose risks to us not encountered in other commercial contracts, including significant regulatory compliance risks. Contracts funded by the U.S. government and its agencies include provisions that reflect the government's substantial public policy and compliance requirements, and 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;
- reduce or modify the government's obligations under such agreements without the consent of the contractor;
- 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 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; and
- pursue criminal or civil remedies under the False Claims Act, or the FCA, the False Statements Act and similar remedy provisions specific to government agreements.

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;
- 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, anti-human-trafficking, non-discrimination and affirmative action programs, energy efficiency and environmental compliance requirements.

If we fail to maintain compliance with these requirements, we may be subject to potential contract or FCA liability and to termination of our contracts.

U.S. government agencies have special contracting requirements that give them the ability to unilaterally control our contracts.

U.S. government contracts typically contain unfavorable termination provisions and are subject to audit and modification by the government at its sole discretion, which will subject us to additional risks. These risks include the ability of the U.S. government to unilaterally:

- audit and object to our government contract-related costs and fees, and require us to reimburse all such costs and fees;
- suspend or prevent us for a set period of time from receiving new contracts or extending our existing contracts based on violations or suspected violations of laws or regulations;
- cancel, terminate or suspend our contracts based on violations or suspected violations of laws or regulations;
- terminate our contracts if in the government's interest, including if funds become unavailable to the applicable governmental agency;
- reduce the scope and value of our contract; and
- change certain terms and conditions in our contract.

The U.S. government will be able to terminate any of its contracts with us, either for convenience or if we default by failing to perform in accordance with or to achieve the milestones set forth in the contract schedules and terms. Termination-for-convenience provisions generally enable us to recover only our costs incurred or committed and settlement expenses on the work completed prior to termination. Except for the amount of services received by the government, termination-for-default provisions do not permit these recoveries and would make us liable for excess costs incurred by the U.S. government in procuring undelivered items from another source.

Our business is subject to audit by the U.S. government and other potential sources for grant funding, including under our contracts with BARDA, NIAID, DoD and CARB-X, and a negative outcome in an audit could adversely affect our business

U.S. government agencies such as the Department of Health and Human Services, or the DHHS, and the Defense Contract Audit Agency, or the DCAA, routinely audit and investigate government contractors. These agencies review a contractor's performance under its contracts, cost structure and compliance with applicable laws, regulations and standards.

The DHHS and the DCAA also review the adequacy of, and a contractor's compliance with, its internal control systems and policies, including the contractor's purchasing, property, estimating, compensation and management information systems. Any costs found to be improperly allocated to a specific contract will not be paid, while such costs already paid must be refunded. If an audit uncovers improper or illegal activities, we may be subject to civil and criminal penalties and administrative sanctions, including:

- termination of contracts;
- forfeiture of profits;
- suspension of payments;
- fines; and
- suspension or prohibition from conducting business with the U.S. government.

In addition, we could suffer serious reputational harm if allegations of impropriety were made against us, which could cause our stock price to decrease.

Laws and regulations affecting government contracts make it more expensive and difficult for us to successfully conduct our business.

We must comply with numerous laws and regulations relating to the formation, administration and performance of government contracts, which can make it more difficult for us to retain our rights under our government contracts. These laws and regulations affect how we conduct business with government agencies. Among the most significant government contracting regulations that affect our business are:

- the Federal Acquisition Regulations, or the FAR, and agency-specific regulations supplemental to the FAR, which comprehensively regulate the procurement, formation, administration and performance of government contracts;
- business ethics and public integrity obligations, which govern conflicts of interest and the hiring of former government employees, restrict the granting of gratuities and funding of lobbying activities and include other requirements such as the Anti-Kickback Statute and the Foreign Corrupt Practices Act;
- export and import control laws and regulations; and
- laws, regulations and executive orders restricting the use and dissemination of information classified for national security purposes and the exportation of certain products and technical data.

These requirements change frequently, such as through appropriations bills or executive orders. Any changes in applicable laws and regulations could restrict our ability to maintain our existing BARDA and other government contracts and obtain new contracts, which could limit our ability to conduct our business and materially adversely affect our results of operations.

Provisions in our U.S. government contracts, including our contracts with BARDA, may affect our intellectual property rights.

Certain of our activities have been funded, and may in the future be funded, by the U.S. government, including through our contracts with BARDA. When new technologies are developed with U.S. government funding, the government obtains certain rights in any resulting patents, including the right to a nonexclusive license authorizing the government to use the invention and rights that may permit the government to disclose our confidential information to third parties and to exercise “march-in” rights. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the U.S. government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U.S. industry. In addition, U.S. government-funded inventions must be reported to the government, U.S. government funding must be disclosed in any resulting patent applications, and our rights in such inventions may be subject to certain requirements to manufacture products in the United States.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient patent protection for our technology or our product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize technology and products 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 proprietary chemistry 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 position, 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 approval process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds and technologies commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Furthermore, recent changes in patent laws in the United States, including the America Invents Act of 2011, may affect the scope, strength and enforceability of our patent rights or the nature of proceedings which may be brought by us related to our patent rights.

Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. 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.

The laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, even assuming the other requirements for patentability are met, currently, in the United States, the first to make the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. 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. As a result of the America Invents Act of 2011, the United States transitioned to a first-inventor-to-file system in March 2013, under which, assuming the other requirements for patentability are met, the first inventor to file a patent application is entitled to the patent. However, as a result of the lag in the publication of patent applications following filing in the United States, we are still not be able to be certain upon filing that we are the first to file for patent protection for any invention. Moreover, we may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, *inter partes* review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, 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. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

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

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

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

If we are sued for infringing intellectual property rights of third parties, or otherwise become involved in disputes regarding our intellectual property rights, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

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 and pending applications 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 or patent applications 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 U.S. Patent and Trademark Office. Intellectual property disputes arise in a number of areas including with respect to patents, use of other proprietary rights and the contractual terms of license arrangements. Third parties may assert claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. With respect to our Meiji License of certain know-how used in tebipenem HBr, we are neither a party to, nor an express third-party beneficiary of, the letter agreement between Meiji and Global Pharma consenting to Meiji's arrangement with us. As such, if any dispute among the parties were to occur, our direct enforcement rights with respect to the letter agreement may be limited or uncertain. A termination or early expiration of the head license between Meiji and Global Pharma (which currently by its terms is set to expire in January 2022) or any restriction on our ability to use the Global Pharma know-how could have a negative impact on our development of tebipenem HBr and adversely affect our business.

If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. 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 be subject to claims that we or our employees, consultants or contractors have misappropriated the intellectual property of a third party, or claims asserting ownership of what we regard as our own intellectual property.

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

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. To the extent that we fail to obtain such assignments or such assignments are breached, we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

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

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, in seeking to develop and maintain a competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our consultants, independent contractors, advisors, corporate collaborators, outside scientific collaborators, contract manufacturers, suppliers and other third parties. We, as well as our licensors, also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

We have registered trademarks and pending trademark applications. Failure to enforce our registered marks or secure registration of our pending trademark applications could adversely affect our business.

We have registered our trademarks for our name and logo in the United States and other countries and have a number of pending trademark applications in the United States and other countries. As of December 31, 2019, Spero therapeutics has two registered U.S. trademarks, nine registered foreign trademarks, and nine pending trademark applications. If our registered trademarks are invalidated, we may be unable to exclusively use our name or logo in certain jurisdictions or may need to change our name or logo in certain jurisdiction, which could affect our business. If we do not secure registrations for our pending trademark applications, we may encounter more difficulty in enforcing them against third parties, which could adversely affect our business. We have not yet registered trademarks for any of our product candidates in any jurisdiction. When we file trademark applications for our product candidates, those applications may not be allowed for registration, and registered trademarks may not be obtained, maintained or enforced. During trademark registration proceedings in the United States and foreign jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but we may not be able to overcome such rejections. In addition, in the United States Patent and Trademark Office and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings.

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

Risks Related to Regulatory Approval and Other Legal Compliance Matters

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

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

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

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

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

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

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

Even if we eventually receive approval of an NDA or foreign marketing application for our product candidates, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials, often referred to as Phase 4 clinical trials, and the FDA may require the implementation of an REMS which may be required to ensure safe use of the drug after approval. The FDA or the applicable foreign regulatory agency also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

A fast track designation may not actually lead to a faster development or regulatory review or approval process.

We have received fast track designation for tebipenem HBr for the treatment of complicated urinary tract infections and acute pyelonephritis and may seek fast track designation for one or more of our other product candidates. If a drug is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a drug sponsor may apply for fast track designation by the FDA for the particular indication under study. If fast track designation is obtained, the FDA may initiate review of sections of an NDA before the application is complete. This "rolling review" is available if the applicant provides and the FDA approves a schedule for the remaining information. If we seek fast track designation for a product candidate, we may not receive it from the FDA. However, even if we receive fast track designation, fast track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with fast track designation compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

In March 2020, the FDA granted orphan drug designation for SPR720. We may seek orphan drug designation for certain of our product candidates. We may not be able to obtain or maintain orphan drug designations for any of our product candidates, and we may be unable to take advantage of the benefits associated with orphan drug designation, including the potential for market exclusivity.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product as an orphan product if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population of greater than 200,000 individuals in the United States, but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. There can be no assurance that the FDA will grant orphan designation for any indication for which we apply.

In the United States, orphan designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product candidate that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, it is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including an NDA, to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity.

Even though we have obtained orphan drug designation for SPR720 and may seek orphan drug designation for other product candidates in the future, there is no assurance that we will be the first to obtain marketing approval for SPR720 or for any particular rare indication. Further, even though we have obtained orphan drug designation for SPR720, or even if we obtain orphan drug designation for other potential product candidates, such designation may not effectively protect us from competition because different drugs can be approved for the same condition and the same drug can be approved for different conditions and potentially used off-label in the orphan indication. Even after an orphan drug is approved, the FDA can subsequently approve a competing drug for the same condition for several reasons, including, if the FDA concludes that the later drug is safer or more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process. ***If we are unable to obtain marketing approval in international jurisdictions, we will not be able to market our product candidates abroad.***

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

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

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

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

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

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

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay marketing approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we may obtain marketing approval. Our future arrangements with third-party payors and customers will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval and reimbursement. These laws and regulations include, for example, the false claims and anti-kickback statutes and regulations. At such time as we market, sell and distribute any products for which we obtain marketing approval and reimbursement, it is possible that our business activities could be subject to challenge under one or more of these laws and regulations. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal healthcare Anti-Kickback Statute, among other things, prohibits persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federally funded healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate the statute in order to have committed a violation. In addition, the government may assert that a claim that includes 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;
- the federal False Claims Act imposes criminal and civil penalties, which can be enforced by private citizens through civil whistleblower and qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, 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 federal ban on physician self-referrals, which prohibits, subject to certain exceptions, physician referrals of Medicare or Medicaid patients to an entity providing certain “designated health services” if the physician or an immediate family member of the physician has any financial relationship with the entity;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or for making any false statements relating to healthcare matters; as in the case of the federal healthcare Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate the statute in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, also imposes obligations on certain covered entities as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, and requires notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency or “sunshine” requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the ACA, requires manufacturers of drugs, devices, biologics and medical supplies to report to the U.S. Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to implement compliance programs and to track and report gifts, compensation and other remuneration provided to physicians, in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and pricing information. State laws also govern the privacy and security of health information in some circumstances, and many such state laws differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

We will be required to spend substantial time and money to ensure that our business arrangements with third parties, and our business generally, comply with applicable healthcare laws and regulations. Even then, governmental authorities may conclude that our business practices, including arrangements we may have with physicians and other healthcare providers, some of whom may receive stock options as compensation for services provided, do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If governmental authorities find that our operations violate 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, damages, imprisonment, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and we may be required to curtail or restructure our operations. Moreover, we expect that there will continue to be federal and state laws and regulations, proposed and implemented, that could affect our operations and business. The extent to which future legislation or regulations, if any, relating to healthcare fraud and abuse laws or enforcement, may be enacted or what effect such legislation or regulation would have on our business remains uncertain.

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

The FDA has established regulations to govern the drug development and approval process, as have foreign regulatory authorities. The policies of the FDA and other regulatory authorities may change and additional laws may be enacted or government regulations may be promulgated that could prevent, limit, delay but also accelerate regulatory review of our product candidates. 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 all of its provisions have not yet been implemented. Among other things, the Cures Act provides a new "limited population" pathway for certain antibacterial and antifungal drugs, or LPAD, but the FDA has not yet issued guidance regarding the LPAD. Additionally, in August 2017, 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 FDA will have on the development of our product candidates.

Recently enacted and future policies and legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the reimbursement made for any product candidate for which we receive marketing approval.

The pricing and reimbursement environment may become more challenging due to, among other reasons, policies advanced by the new presidential administration, federal agencies, new healthcare legislation passed by the U.S. Congress or fiscal challenges faced by all levels of government health administration authorities. Among policy makers and payors in the United States and foreign countries, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of any products for which we obtain marketing approval, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals. Resulting legislative, administrative, or policy changes from payors may reduce payments for any products for which we obtain marketing approval and could affect future revenues.

The ACA became law in the United States in March 2010 with the goals of broadening access to health insurance, reducing or constraining the growth of healthcare spending, enhancing remedies against fraud and abuse, adding new transparency requirements for the health care and health insurance industries and imposing additional health policy reforms. Provisions of ACA may negatively affect our future revenues. For example, the ACA requires, among other things, that annual fees be paid by manufacturers for certain branded prescription drugs, that manufacturers participate in a discount program for certain outpatient drugs under Medicare Part D, and that manufacturers provide increased rebates under the Medicaid Drug Rebate Program for outpatient drugs dispensed to Medicaid recipients. The ACA also addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for line extensions and expands oversight and support for the federal government's comparative effectiveness research of services and products.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. As a result, there have been delays in the implementation of certain aspects of the ACA. Both Congress and President Trump have expressed their intention to repeal or repeal and replace the ACA, and as a result certain sections of the ACA have not been fully implemented or effectively repealed. The uncertainty around the future of the ACA, and in particular the impact to reimbursement levels, may lead to uncertainty or delay in the purchasing decisions of our customers, which may in turn negatively impact our product sales. If there are not adequate reimbursement levels, our business and results of operations could be adversely affected.

Beginning on April 1, 2013, Medicare payments for all items and services under Part A and B, including drugs and biologicals, and most payments to plans under Medicare Part D were reduced by 2%, or automatic spending reductions, required by the Budget Control Act of 2011, or BCA, as amended by the American Taxpayer Relief Act of 2012. The BCA requires sequestration for most federal programs, excluding Medicaid, Social Security, and certain other programs. The BCA caps the cuts to Medicare payments for items and services and payments to Part D plans at 2%. Subsequent legislation extended the 2% reduction, on average, to 2025. As long as these cuts remain in effect, they could adversely affect payment for our product candidates. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. There have been several U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical 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.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. 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 effect 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.

If we successfully commercialize one of our product candidates, failure to comply with our reporting and payment obligations under U.S. governmental pricing programs could have a material adverse effect on our business, financial condition and results of operations.

If we participate in the Medicaid Drug Rebate Program if and when we successfully commercialize a product candidate, we will be required to report certain pricing information for our product to the Centers for Medicare & Medicaid Services, the federal agency that administers the Medicaid and Medicare programs. We may also be required to report pricing information to the U.S. Department of Veterans Affairs. If we become subject to these reporting requirements, we will be liable for errors associated with our submission of pricing data, for failure to report pricing data in a timely manner, and for overcharging government payers, which can result in civil monetary penalties under the Medicaid statute, the federal civil False Claims Act, and other laws and regulations.

Our employees, independent contractors, principal investigators, contract research organizations, consultants or vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

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

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the "Tax Cuts and Jobs Act," or TCJA, which significantly reforms the Internal Revenue Code of 1986, as amended. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and puts into effect the migration from a "worldwide" system of taxation to a territorial system. As a result of the TCJA, our net deferred tax assets and liabilities existing as of December 31, 2017 were revalued at the newly enacted U.S. corporate rate. The impact of this tax reform is uncertain and could be adverse. We urge our investors to consult with their legal and tax advisors with respect to such legislation and the potential tax consequences of investing in our securities.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent our product candidates from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business relies, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly affect the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Risks Related to Employee Matters and Managing Growth

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

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Ankit Mahadevia, M.D., our President and Chief Executive Officer, as well as the other principal members of our management, scientific and clinical team. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time.

If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize product candidates successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

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

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

If foreign approvals are obtained, we will be subject to additional risks in conducting business in international markets.

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

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

These and other risks may materially adversely affect our ability to attain or sustain revenue from international markets.

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

In the future, we may enter into transactions to acquire other businesses, products or technologies. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Risks Related to Our Common Stock

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for our stockholders.

Our stock price may be volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their shares at or above the price they paid for their shares. The market price for our common stock may be influenced by many factors, including:

- the success of existing or new competitive products or technologies;
- the timing of clinical trials of tebipenem HBr and any other product candidate;
- results of clinical trials of tebipenem HBr and any other product candidate;
- failure or discontinuation of any of our development programs;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- the perception of the pharmaceutical and biotechnology industry by the public, legislatures, regulators and the investment community;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to develop, in-license or acquire additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

In addition, the stock market has experienced significant volatility, particularly with respect to pharmaceutical, biotechnology and other life sciences company stocks. The volatility of pharmaceutical, biotechnology and other life sciences company stocks often does not relate to the operating performance of the companies represented by the stock. In the past, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management’s attention and resources, and could also require us to make substantial payments to satisfy judgments or to settle litigation.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock relies in part on the research and reports that securities or industry analysts publish about us or our business. If few analysts provide coverage of us, the trading price of our stock would likely decline. If one or more of the analysts covering our business downgrade our stock or change their opinion of our stock, our share price would likely decline. In addition, if one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

We can issue and have issued shares of preferred stock, which may adversely affect the rights of holders of our common stock.

Our amended and restated certificate of incorporation authorizes us to issue up to 10,000,000 shares of preferred stock with designations, rights and preferences determined from time-to-time by our board of directors. Accordingly, our board of directors is empowered, without stockholder approval, to issue preferred stock with dividend, liquidation, conversion, voting or other rights superior to those of holders of our common stock. For example, an issuance of shares of preferred stock could:

- adversely affect the voting power of the holders of our common stock;
- make it more difficult for a third party to gain control of us;
- discourage bids for our common stock at a premium;
- limit or eliminate any payments that the holders of our common stock could expect to receive upon our liquidation; or
- otherwise adversely affect the market price or our common stock.

We have in the past issued, and we may at any time in the future issue, shares of preferred stock. In connection with our July 2018 public offering, we issued 2,220 shares of our Series A Convertible Preferred Stock, or Series A Preferred Stock, to certain affiliates of Biotechnology Value Fund, L.P., or BVF, each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. In November 2018, we entered into an exchange agreement with BVF to exchange 1,000,000 shares of our common stock previously held by BVF for 1,000 shares of our Series B Convertible Preferred Stock, or Series B Preferred Stock, each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. In June 2019, BVF converted 500 shares of Series A Convertible Preferred Stock into 500,000 shares of our common stock pursuant to BVF's rights under the certificate of designation for such Series A Convertible Preferred Stock. In connection with our rights offering, which we launched in February 2020 and closed in early March 2020, we issued 2,287 shares of our Series C Convertible Preferred Stock to BVF. If BVF or any other future holders of our shares of preferred stock convert their shares into common stock, existing holders of our common stock will experience dilution.

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

Our management will have broad discretion in the application of our cash reserves, including the proceeds from our July 2018 equity offering, and could spend these funds 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 material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash reserves in a manner that does not produce income or that loses value.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock 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 may remain an emerging growth company for up to five years. We would cease to be an emerging growth company upon the earlier of: (i) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of our IPO, which is December 31, 2022; (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC which means the first day of the year following the first year in which the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of June 30th. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or Sarbanes-Oxley, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and we will therefore be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, changes in rules of U.S. generally accepted accounting principles or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an "emerging growth company," we incur significant legal, accounting and other expenses that we did not incur as a private company. Sarbanes-Oxley, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly. For example, these rules and regulations have made it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. 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.

Failure to maintain effective internal controls in accordance with Section 404 of Sarbanes-Oxley in the future could have a material adverse effect on our ability to produce accurate financial statements and on our stock price.

Section 404 of Sarbanes-Oxley requires us, on an annual basis, to review and evaluate our internal controls. To maintain compliance with Section 404, we are required to document and evaluate our internal control over financial reporting, which is both costly and challenging. We will need to continue to dedicate internal resources, continue to engage outside consultants and follow a detailed work plan to continue to assess and document the adequacy of internal control over financial reporting, continue 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. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

A significant portion of our total outstanding shares may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Our outstanding shares of common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act of 1933, as amended, or the Securities Act, or to the extent that such shares have already been registered under the Securities Act and are held by non-affiliates of ours. Moreover, holders of a substantial number of shares of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also have registered all shares of common stock that we may issue under our equity compensation plans or that are issuable upon exercise of outstanding options. These shares can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the operation, development and growth of our business. To the extent that we enter into any future debt agreements, the terms of such agreements may also preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

Our executive officers, directors and principal stockholders maintain the ability to control all matters submitted to stockholders for approval.

As of December 31, 2019, our executive officers and directors, combined with our stockholders who as of such date owned more than 5% of our outstanding common stock, in the aggregate, beneficially own shares representing approximately 44% of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and/or our board of directors; or
- impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, 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 amended and restated by-laws may discourage, delay or prevent a merger, acquisition or other change in control of us that our stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also 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 all members of the board are not elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call a special meeting of stockholders;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “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 75% of the votes that all of our stockholders would be entitled to cast to amend or repeal certain provisions of our certificate of incorporation or by-laws.

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 in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our headquarters are located in Cambridge, Massachusetts, where we lease approximately 23,400 square feet of office space. Our lease extends through May 2027. We believe that our existing facilities will be sufficient to meet our current needs.

Item 3. Legal Proceedings.

We are not party to any material legal proceedings.

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 has been publicly traded on The Nasdaq Global Select Market under the symbol "SPRO" since the initial public offering of our common stock on November 2, 2017. Prior to that time, there was no public market for our common stock.

Holders of Record

As of March 9, 2020, we had approximately 11 stockholders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

Dividends

We have never declared or paid cash dividends on our capital stock since our inception. We currently intend to retain all available funds and future earnings, if any, for use in the operation of our business and do not anticipate paying any cash dividends on our common stock in the foreseeable future. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, our financial condition, our capital requirements, general business conditions, our future prospects and other factors that our board of directors may deem relevant. Additionally, our ability to pay dividends on our capital stock could be limited by terms and covenants of any future indebtedness.

Purchases of Equity Securities by the Issuer

None.

Item 6. Selected Financial Data.

Not applicable.

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

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

Overview

We are a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing and commercializing treatments in high unmet need areas involving multi-drug resistant, or MDR, bacterial infections and rare diseases. Our most advanced product candidate, tebipenem pivoxil hydrobromide, or tebipenem HBr (previously SPR994), is designed to be the first broad-spectrum oral carbapenem-class antibiotic for use in adults to treat multi-drug resistant, or MDR, Gram-negative infections. Treatment with effective orally administrable antibiotics may prevent hospitalizations for serious infections and enable earlier, more convenient and cost-effective treatment of patients after hospitalization. We are also developing SPR720, a novel oral antibiotic designed for the treatment of non-tuberculous mycobacterial, or NTM, disease, a rare, orphan disease caused by pulmonary non-tuberculous mycobacterial infections. In addition, we also have a platform technology known as our Potentiator Platform, which includes an intravenous, or IV,-administered product candidate, SPR206, which is being developed to treat MDR Gram-negative infections in the hospital. We believe that our novel product candidates, if successfully developed and approved, would have a meaningful patient impact and significant commercial applications for the treatment of MDR infections in both the community and hospital settings. Since our inception in 2013, we have focused substantially all of our efforts and financial resources on organizing and staffing our company, business planning, raising capital, acquiring and developing product and technology rights, building our intellectual property portfolio and conducting research and development activities for our product candidates. We do not have any products approved for sale and have not generated any revenue from product sales.

We have experienced net losses and significant cash outflows from cash used in operating activities since our inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. As of December 31, 2019, we had an accumulated deficit of $199.4 million, and cash, cash equivalents and marketable securities of $82.0 million. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. Based on our current plans, we believe that our existing cash, cash equivalents and marketable securities, together with the committed funding from our existing BARDA contract and other non-dilutive funding commitments, together with the net proceeds from our rights offering completed in early March 2020, will enable us to fund our operating expenses and capital expenditure requirements into the first quarter of 2021, including through the filing of an NDA for Tebipenem HBr. Because these funds will not sufficient to fund our operations, as currently planned, for more than one year beyond the filing date of this Annual Report on Form 10-K, we have determined that there is substantial doubt regarding our ability to continue as a going concern. We will require additional funding to fund the development of our product candidates through regulatory approval and commercialization, and to support our continued operations. There is no assurance that we will be successful in obtaining sufficient funding on acceptable terms, if at all and we could be forced to delay, reduce or eliminate some or all of our research and development programs, product portfolio expansion or commercialization efforts, which could materially adversely affect our business prospects or our ability to continue operations.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for our product candidates. If we obtain regulatory approval for any of our product candidates and do not enter into a commercialization partnership, we expect to incur significant expenses related to developing our internal commercialization capability to support product sales, marketing and distribution. Further, we expect to incur additional costs associated with our continued operation as a public company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, government funding arrangements, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates.

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

Recent Developments

Closing of Rights Offering for Net Proceeds of Approximately $29.5 Million

On March 5, 2020, we closed our previously announced rights offering issuing 1,046,249 shares of common stock and 2,287 shares of Series C Preferred Stock raising net proceeds of approximately $29.5 million.

Tebipenem HBr – Positive recommendation from independent data review committee regarding pivotal Phase 3 clinical trial and exercise of $15.9 million option by BARDA for tebipenem HBr development

On October 3, 2019, we announced that an independent review committee evaluated interim pharmacokinetic plasma data following the first 70 patients enrolled in our ongoing ADAPT-PO pivotal Phase 3 clinical trial of tebipenem HBr, our oral carbapenem product candidate, and recommended that we continue the trial without modification of the protocol-defined dose. The independent review committee reviewed interim plasma concentration data from the first 33 patients who were randomized to tebipenem HBr in the Phase 3 clinical trial for the treatment of complicated urinary tract infections, or cUTI, and acute pyelonephritis, or AP. A primary objective of the independent review committee was to confirm that plasma levels of tebipenem HBr in patients in the Phase 3 clinical trial support the selected treatment dose. The Phase 3 trial remains blinded and will continue as planned. ADAPT-PO is designed as a double-blind, double-dummy clinical trial to compare oral tebipenem HBr dosed as 600 mg administered three times per day, or TID, with a standard of care IV-administered antibiotic, ertapenem, in approximately 1,200 patients with cUTI or AP, randomized 1:1 in each arm. We expect to report top-line data from the Phase 3 clinical trial in the third quarter of 2020.

On February 5, 2020, we announced that the Biomedical Advanced Research and Development Authority (BARDA) exercised its first contract option for additional committed funding pursuant to its existing contract with Spero. Specifically, the option exercise provides us with $15.9 million in reimbursement for the further development of tebipenem HBr. The $15.9 million option exercise is expected to support the funding of specified manufacturing activities required for approval of tebipenem HBr including active pharmaceutical ingredient, or API, validation batch manufacturing and stability studies. Additionally, the option is expected to support the funding of several non-clinical and clinical development activities including a Phase 1 bronchoalveolar lavage, or BAL, study in healthy subjects that we anticipate initiating in the third quarter of 2020, as well as non-human primate efficacy studies in one or more models of biothreat disease. The option was exercised under Spero's existing 2018 contract with BARDA, which provides for reimbursement to us of up to $46.8 million for qualified expenses for tebipenem HBr development over a five-year period. Total committed funding under the BARDA award to date is $34.1 million, inclusive of the first contract option exercised in 2020. There is a second option exercisable by BARDA for the remaining $12.7 million of funding, subject to specified milestones being achieved under the award agreement. Furthermore, the Defense Threat Reduction Agency (DTRA) provides up to $10.0 million, in addition to the total potential award from BARDA, to cover the cost of the nonclinical biodefense aspects of the collaboration program for tebipenem HBr.

SPR720 – First indication of human safety and PK profiles for SPR720 supports advancement of program to a Phase 2a proof-of-concept clinical trial in patients planned to initiate in the second half of 2020

On December 4, 2019, we announced preliminary findings from our Phase 1 first-in-human clinical trial of SPR720. Analysis of blinded data from the Phase 1 double-blind, placebo-controlled single ascending dose, or SAD, and multiple ascending dose, or MAD, clinical trial in healthy volunteers suggests that SPR720 is generally well-tolerated, with a pharmacokinetic, or PK, profile that we believe supports the further development of SPR720 as an oral agent for the treatment of NTM disease. Specifically, there were no serious adverse events reported and all participants completed the trial. An analysis of preliminary data indicates that SPR720 was generally well-tolerated at doses up to 1000 mg over the maximum studied duration of 14 days. Preliminary analyses of PK data across the cohorts show no significant impact of either advanced age or administration with food on PK variables. At doses of 500 mg or higher, the mean plasma drug exposures of SPR719, the active metabolite of SPR720, are consistent with those suggested by in vitro and in vivo models of SPR720 to be necessary for clinical efficacy against target NTM pathogens. In early February 2020 the SPR720 Phase 1 clinical trial was unblinded and the findings are in line with the preliminary analysis. We plan to submit an Investigational New Drug Application, or IND, to the FDA and initiate a Phase 2a clinical trial of SPR720 in patients with NTM disease during the second half of 2020.

Potentiator Platform – Based on preliminary findings from Phase 1 clinical trial, we have selected SPR206 as lead product candidate within Potentiator Platform, and discontinued development of SPR741

On January 13, 2020, we announced preliminary findings from our Phase 1 first-in-humans clinical trial of SPR206. Analysis of preliminary, blinded data from the Phase 1 double-blind, placebo-controlled SAD and MAD clinical trial in healthy adult volunteers suggests that SPR206 is well-tolerated at doses that are likely to be within a therapeutic range for target MDR Gram-negative bacterial infections and has a safety profile that we believe supports the further development of SPR206. The decision to continue development of SPR206 is also supported by data from nonclinical studies in which SPR206 demonstrated activity as a single agent against MDR and extensively drug resistant, or XDR, bacterial strains, including isolates of *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and carbapenem-resistant *Enterobacteriaceae*, in both *in vitro* and *in vivo* models of infection.

The Phase 1 clinical trial of SPR206 (Study SPR206-101) evaluated the safety, tolerability and pharmacokinetics of intravenously administered SPR206 at single doses ranging from 10 mg to 400 mg in seven SAD cohorts and repeat total daily doses ranging from 75 mg to 450 mg for seven consecutive days and 300 mg for 14 consecutive days across five MAD cohorts. A total of 96 healthy volunteers were randomized to receive SPR206 or placebo. All reported adverse events were mild to moderate and there were no reported severe or serious adverse events. No evidence of nephrotoxicity was observed and there were no subjects with clinically significant changes in laboratory tests during the study. Although the data remain blinded, an analysis of preliminary data indicates that SPR206 was well-tolerated at doses up to 100 mg administered three-times a day, a total of 300 mg daily, for 14 consecutive days. Preliminary analyses of pharmacokinetic data across the cohorts indicates dose linearity and dose proportionality as well as mean plasma drug exposures of SPR206 that are concordant with preclinical models predictive for clinical efficacy against target Gram-negative pathogens.

We expect to receive a development milestone payment from our partner Everest Medicines upon delivery of the SPR206-101 SAD/MAD clinical study report, or CSR, as specified under the regional collaboration launched in 2019 and expects to present final data from the Phase 1 clinical trial in the first half of 2020. In conjunction with Everest Medicines, and through its grant from DoD awarded in July 2019, we plan to conduct a Phase 1 BAL clinical trial assessing the penetration of SPR206 into the pulmonary compartment in the second half of 2020 as well as initiate a renal impairment study of SPR206.

Based on the foregoing, we have determined to discontinue development of SPR741, effective January 1, 2020. We believe that the collective data from the recent Phase 1 and preclinical studies suggest a potency and safety profile for SPR206 that may be superior to SPR741. Further, we believe SPR206 may have a potentially faster path to pivotal clinical trials when compared with SPR741 because SPR206 is being developed as a single agent. As a result of this decision, we have terminated our license agreement with Northern Antibiotics Oy (Ltd.) relating to SPR741. Effective January 1, 2020, the intellectual property rights associated with SPR741 have entirely reverted to Northern Antibiotics and we no longer have any rights with respect thereto and we no longer have any obligations for the cost of maintaining such intellectual property.

Components of Our Results of Operations

Grant Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval, we may generate revenue in the future from product sales. We cannot predict if, when, or to what extent we will generate revenue from the commercialization and sale of our product candidates. We may never succeed in obtaining regulatory approval for any of our product candidates.

To date, the majority of our revenue has been derived from government awards. We expect that our revenue for the next several years will be derived primarily from payments under our government awards that we have currently entered into and that we may enter into in the future.

Collaboration Revenue

Collaboration revenue relates to our agreement with Everest Medicines.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of our product candidates, which include:

- employee-related expenses, including salaries, related benefits, travel and share-based compensation expense for employees engaged in research and development functions;
- expenses incurred in connection with the preclinical and clinical development of our product candidates, including under agreements with contract research organizations, or CROs;
- costs incurred in connection with our government awards;
- the cost of consultants and contract manufacturing organizations, or CMOs, that manufacture drug products for use in our preclinical studies and clinical trials;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and supplies; and
- payments made under third-party licensing agreements.

Prior to novation of the NIAID contract to us in December 2017, under our agreements with PBB and certain of its affiliates, CAI continued to perform research and development at our direction. We paid CAI for such research and development services at an agreed-upon rate that took into consideration costs incurred by CAI, net of amounts reimbursed to CAI by NIAID. Thus, prior to novation of the NIAID contract to us in December 2017, the amount we record as research and development expenses is net of the NIAID reimbursement amount that CAI received. We also paid CAI a portion of the NIAID reimbursement received at rates specified in the agreement, which we also recorded as research and development expense.

Since the fourth quarter of 2016, we have recorded research and development expenses conducted by our Australian subsidiary net of a 43.5% research and development tax incentive we expect to receive for qualified expenses from the Australian government.

As described above, in June 2019, we entered into a collaboration with the Bill and Melinda Gates Medical Research Institute (the “Gates MRI”), a nonprofit research institution wholly owned by the Bill and Melinda Gates Foundation. Gates MRI will conduct and fund preclinical and clinical studies for the development of SPR720 against tuberculosis, or TB, and also fund certain agreed upon collaborative research activities performed by us. Due to our assessment that we do not have a vendor/customer relationship with the Gates MRI, we recognize the funding received under the agreement as a reduction to the research and development expenses as the related expenses are incurred.

We expense research and development costs as incurred. Nonrefundable advance payments we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed.

Our direct research and development expenses are tracked on a program-by-program basis and consist primarily of external costs, such as fees paid to consultants, contractors, CMOs and CROs in connection with our preclinical and clinical development activities. License fees and other costs incurred after a product candidate has been designated and that are directly related to the product candidate are included in direct research and development expenses for that program. License fees and other costs incurred prior to designating a product candidate are included in early stage research programs. We do not allocate employee costs, costs associated with our preclinical programs or facility expenses, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple product development programs and, as such, are not separately classified.

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will increase substantially in connection with our ongoing and planned clinical development activities in the near term and in the future as we progress our existing clinical trials and other studies of tebipenem HBr, SPR720 and SPR206, continue to discover and develop additional product candidates, hire additional clinical and scientific personnel and acquire or in-license other product candidates and technologies.

At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any of our product candidates. The successful development and commercialization of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties, including the following:

- successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers to obtain manufacturing supply;
- obtainment and maintenance of patent, trade secret protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain our license agreement with Meiji with respect to tebipenem HBr;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales of tebipenem HBr and our other product candidates, if approved, whether alone or in collaboration with others;
- acceptance of tebipenem HBr and our other product candidates, if approved, by patients, the medical community and third-party payors;
- competition with other therapies; and
- a continued acceptable safety profile of tebipenem HBr and our other product candidates, if approved.

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 may never succeed in obtaining regulatory approval for any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs, including share-based compensation, for personnel in executive, finance and administrative functions. General and administrative expenses also include direct and allocated facility-related costs as well as professional fees for legal, patent, consulting, investor and public relations, 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 of our product candidates. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance, infrastructure, and director and officer insurance costs as well as investor and public relations expenses associated with our continued operation as a public company.

Other Income (Expense)

Anti-Dilution Rights. In connection with the issuance of non-controlling interests in certain of our subsidiaries, specifically Spero Gyrase, Inc., we granted the minority investors the right to maintain ownership interests at no additional cost, subject to a maximum ownership percentage, which rights we refer to collectively as anti-dilution rights. We classified the anti-dilution rights as derivative liabilities on our consolidated balance sheet that we remeasured to fair value at each reporting date, and we recognized changes in the fair value of the derivative liabilities associated with the anti-dilution rights as a component of other income (expense) in our consolidated statement of operations and comprehensive loss. In May 2017, we repurchased 100% of the minority investor's outstanding shares in Spero Europe, Ltd. and settled the anti-dilution rights associated with the shares. In December 2019, we repurchased 100% of the minority investor's outstanding shares in Spero Gyrase, Inc. at a price of $0.001 per share. As a result, as of December 31, 2019, there are no anti-dilution rights outstanding.

Interest Income and Other Income (Expense), Net

Interest income consists of interest earned on our cash equivalents, which are primarily invested in money market accounts, as well as interest earned on our investments in marketable securities that we held during the years ended December 31, 2019 and 2018. Other income (expense), net, consists of insignificant amounts of miscellaneous income, as well as realized and unrealized gains and losses from foreign currency-denominated cash balances, vendor payables and receivables from the Australian research and development tax incentive.

Income Taxes

Since our inception, we have not recorded any income tax benefits for the net losses we have incurred in each year or for our earned research and development tax credits, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating loss carryforwards and tax credits will not be realized. As of December 31, 2019, we had federal and state net operating loss carryforwards of $156.8 million and $157.8 million, respectively, which may be available to offset future income tax liabilities. The federal NOLs of $73.0 million will expire at various dates from 2033 to 2037 and approximately $83.8 million can be carried forward indefinitely. The state NOLs begin to expire in 2033 and will expire at various dates through 2039. In addition, as of December 31, 2019, we had foreign net operating loss carryforwards of $7.7 million, which may be available to offset future income tax liabilities and do not expire. As of December 31, 2019, we also had federal and state research and development tax credit carryforwards of $4.1 million and $1.1 million, respectively, which begin to expire in 2033 and 2028, respectively. We have recorded a full valuation allowance against our net deferred tax assets at each balance sheet date.

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, or GAAP. The preparation of our consolidated financial statements and related disclosures requires us to make estimates, assumptions and judgments that affect the reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. 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.

We believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Funding Received from Government Contracts, Tax Incentives and Collaborations

Since our inception, we have been able to obtain partial funding for our research and development activities from government contracts, government tax incentives and a collaboration arrangement. The classification within our statement of operations and comprehensive loss of the funding received under these arrangements is subject to management judgment based on the nature of the arrangements we enter into, the source of the funding and whether the funding is considered central to our business operations.

Government Contracts

We generate revenue from government contracts that reimburse us for certain allowable costs for funded projects. We have determined that government grant revenue is outside the scope of ASC 606. For contracts with government agencies, when we have concluded that we are the principal in conducting the research and development expenses and where the funding arrangement is considered central to our ongoing operations, we classify the recognized funding received as revenue.

We recognize funding received from the Biomedical Advanced Research and Development Authority, or BARDA, the U.S. Department of Defense, or the DoD, the National Institute of Allergy and Infectious Diseases, or NIAID, of the National Institutes of Health, or NIH, and Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, as revenue, rather than as a reduction of research and development expenses, because we are the principal in conducting the research and development activities and these contracts are central to our ongoing operations. We recognize revenue only after the qualifying expenses related to the contracts have been incurred and we are reasonably assured that the expenses will be reimbursed and of the collectability of the revenue. We record revenue recognized upon incurring qualifying expenses in advance of billing as unbilled revenue, which is included in other receivables in our consolidated balance sheet. The related costs incurred by us are included in research and development expense in our consolidated statements of operations and comprehensive loss.

Government Tax Incentives

For available government tax incentives that we may earn without regard to the existence of taxable income and that require us to forego tax deductions or the use of future tax credits and net operating loss carryforwards, we classify the funding recognized as a reduction of the related qualifying research and development expenses incurred.

Since the fourth quarter of 2016, our operating subsidiary in Australia has met the eligibility requirements to receive a 43.5% tax incentive for qualifying research and development activities. We recognize these incentives as a reduction of research and development expenses in our consolidated statements of operations in the same period that the related qualifying expenses are incurred. Reductions of research and development expense recognized upon incurring qualifying expenses in advance of receipt of tax incentive payments are recorded in our consolidated balance sheet as tax incentive receivables. Related to these incentives, we recognized reductions of research and development expense of $0.4 million and $1.2 million during the years ended December 31, 2019 and 2018, respectively.

Collaboration Agreements

For collaboration agreements with a third party, to determine the appropriate statement of operations classification of the recognized funding, we first assess whether the collaboration arrangement is within the scope of the accounting guidance for collaboration arrangements. If it is, we evaluate the collaborative arrangement for proper classification in the statement of operations based on the nature of the underlying activity and we assess the payments to and from the collaborative partner. If the payments to and from the collaborative partner are not within the scope of other authoritative accounting guidance, we base the statement of operations classification for the payments received on a reasonable, rational analogy to authoritative accounting guidance, applied in a consistent manner. Conversely, if the collaboration arrangement is not within the scope of accounting guidance for collaboration arrangements, we assess whether the collaboration arrangement represents a vendor/customer relationship. If the collaborative arrangement does not represent a vendor/customer relationship, we then classify the funding payments received in the statement of operations and comprehensive loss as a reduction of the related expense that is incurred.

In June 2019, we entered into a collaboration agreement with the Gates MRI and concluded that the agreement is within the scope of the accounting guidance for collaboration arrangements. Due to the cost-funded nature of the payments and our assessment that we do not have a vendor/customer relationship with the Gates MRI, we will recognize the funding received under the agreement as a reduction to research and development expense as we incur the related expenses.

Accrued Research and Development Expenses

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

- vendor in connection with the preclinical development activities;
- CMOs in connection with the production of preclinical and clinical trial materials;
- CROs in connection with preclinical and clinical studies; and
- investigative sites in connection with clinical trials.

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

Share-Based Compensation

We measure all share-based awards granted to employees and directors based on the fair value on the date of grant using the Black-Scholes option-pricing model, and we recognize compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. Generally, we issue awards with only service-based vesting conditions and record the expense for these awards using the straight-line method. The Black-Scholes option-pricing model uses as inputs the fair value of our common stock or common units and assumptions we make for the volatility of our common stock or common units, the expected term of our common stock options and incentive units, the risk-free interest rate for a period that approximates the expected term of our common stock options and incentive units, and our expected dividend yield.

Results of Operations

Our financial statements have been presented on the basis that we are a going concern, which contemplates the realization of revenues and the satisfaction of liabilities in the normal course of business. We have incurred losses from the inception of our operations. These factors raise substantial doubt about our ability to continue as a going concern.

Comparison of the Years Ended December 31, 2019 and 2018

The following table summarizes our results of operations for the years ended December 31, 2019 and 2018:

	Year Ended December 31,		
	2019	2018	$ Change
Revenues:			
Grant revenue	$ 13,405	$ 3,966	$ 9,439
Collaboration revenue	4,742	—	4,742
Total revenues	18,147	3,966	14,181
Operating expenses:			
Research and development	65,775	33,885	31,890
General and administrative	15,588	12,887	2,701
Total operating expenses	81,363	46,772	34,591
Loss from operations	(63,216)	(42,806)	(20,410)
Other income (expense):			
Interest income and other income (expense), net	2,291	1,144	1,147
Total other income (expense), net	2,291	1,144	1,147
Net loss	$ (60,925)	$ (41,662)	$ (19,263)

Grant Revenue

	Year Ended December 31,		
	2019	2018	$ Change
BARDA Contract (Tebipenem HBr)	$ 12,082	$ 1,373	$ 10,709
NIAID Contract (SPR206)	1,021	1,356	(335)
NIAID Award (SPR720)	77	490	(413)
DoD Agreement (Potentiator Platform)	225	282	(57)
CARB-X Award (SPR741)	—	465	(465)
Total revenue	$ 13,405	$ 3,966	$ 9,439

Grant revenue recognized during 2019 and 2018 consisted of the reimbursement of qualifying expenses incurred in connection with our various government awards. The increase in revenue during 2019 was primarily due to funding received under our BARDA contract, which was awarded to us in July 2018, and for which we began incurring qualified expenses in the second half of 2018. Offsetting this increase, we received lower funding from our other government contracts and awards, as well as our CARB-X award, which had a performance period through March 31, 2018.

Research and Development Expenses

	Year Ended December 31,		
	2019	2018	$ Change
Direct research and development expenses by program:			
Tebipenem HBr	$ 43,440	$ 11,412	$ 32,028
SPR720	3,741	2,579	1,162
Potentiator Platform (SPR206 and SPR741)	3,617	8,265	(4,648)
Unallocated expenses:			
Personnel related (including share-based compensation)	10,967	8,027	2,940
Facility related and other	4,010	3,602	408
Total research and development expenses	$ 65,775	$ 33,885	$ 31,890

Direct costs related to our tebipenem HBr program increased during 2019 compared to 2018 due to an increase of $26.9 million in clinical trial expenses related to the ADAPT-PO pivotal Phase 3 clinical trial of tebipenem HBr, for which activities began in 2018 and enrollment initiated in the first quarter of 2019. In addition to these higher clinical trial costs, we have incurred higher expenses during 2019 related to formulation development, manufacturing process and manufacturing of clinical trial material. Additionally, during 2018, research and development expenses for our tebipenem HBr program conducted by our Australian subsidiary were recorded net of a 43.5% research and development tax incentive for qualified expenses from the Australian government of $0.9 million. We expect direct costs related to tebipenem HBr to continue to increase as we conclude our pivotal Phase 3 clinical trial and incur expenses related to a potential NDA filing for tebipenem HBr.

Direct costs related to our SPR720 program increased during 2019 compared to 2018 due to the cost of running the Phase 1 clinical trial of SPR720, which we initiated in January 2019, as well as costs related to drug substance and formulation development. Direct costs related to our SPR720 program were recorded net of a $1.7 million reduction in expenses that were funded under our collaboration with Gates MRI. We expect direct costs related to our SPR720 program to continue to increase as we advance this product candidate.

Direct costs related to our Potentiator Platform include costs related to our SPR206 and SPR741 programs. Direct costs related to our SPR206 program decreased by $3.8 million during 2019 as compared to 2018, due to toxicology studies and manufacturing costs incurred in 2018 to prepare for the Phase 1 study of SPR206, which we initiated in December 2018, as well as $0.2 million in expense related to the achievement of regulatory milestones for SPR206 in the fourth quarter of 2018. These prior year expenses were partially offset by higher clinical trial costs in the current year due to the cost of running the Phase 1 trial. We expect direct costs related to our SPR206 program to continue as we advance the program under the DoD award. We incurred minimal expenses related to SPR741 during 2019 and have determined to discontinue this program effective January 1, 2020.

The increase in personnel-related costs included in unallocated expenses of $2.9 million was due to an increase in research and development headcount, as well as a $0.5 million increase in share-based compensation.

The increase in facility-related and other costs was primarily due to the increased costs of supporting a larger group of research and development personnel and their research efforts.

General and Administrative Expenses

	Year Ended December 31,		
	2019	2018	$ Change
Personnel related (including share-based compensation)	$ 8,050	$ 6,751	$ 1,299
Professional and consultant fees	5,849	4,815	1,034
Facility related and other	1,689	1,321	368
Total general and administrative expenses	$ 15,588	$ 12,887	$ 2,701

The increase in personnel-related costs of $1.3 million was primarily a result of an increase in headcount in our general and administrative function as we operate as a public company, as well as a $0.5 million increase in share-based compensation expense.

The increase in professional and consultant fees of $1.0 million was primarily related to increased expenses related to business development and commercial readiness activities.

The increase in facility-related and other costs was primarily due to the increased costs of supporting a larger number of general and administrative personnel.

Other Income (Expense), Net

Other income, net was $2.3 million during 2019, compared to $1.1 million during 2018. Other income, net, for the year ended December 31, 2019 consisted of other income of $2.1 million, which was primarily related to interest income on our invested cash balances and marketable securities, as well as $0.2 million in connection with the repurchase of Vaxart Inc.'s outstanding shares in Spero Gyrase, Inc. at a price of $0.001 per share. Other income, net for the year ended December 31, 2018 consisted of other income of $1.8 million, which was primarily related to interest income on our invested cash balances and marketable securities, partially offset by $0.7 million of other expenses.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We have generated limited revenue to date from funding arrangements with the DoD, NIAID, CARB-X and BARDA and our license agreement with Everest Medicines. We have not yet commercialized any of our product candidates and we do not expect to generate revenue from sales of any product candidates for several years, if at all. To date, we have funded our operations with proceeds from the sales of preferred units and bridge units, payments received under license and collaboration agreements and funding from government contracts, with proceeds from the IPO of our common stock, an underwritten public offering of our common and preferred stock in July 2018, and subsequent sales of our common stock. As of December 31, 2019, we had cash, cash equivalents and marketable securities of $82.0 million.

On December 3, 2018, we filed a universal shelf registration statement on Form S-3 (Registration No. 333-228661) with the SEC, which was declared effective on December 11, 2018, and pursuant to which we registered for sale up to $200.0 million of any combination of our common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that we may determine, including up to $50.0 million of our common stock available for issuance pursuant to an at-the-market offering program sales agreement that we entered into with Cantor Fitzgerald & Co. Under the sales agreement, Cantor may sell shares of our common stock by any method permitted by law deemed to be an “at the market” offering as defined in Rule 415 of the Securities Act, subject to the terms of the sales agreement. During the year ended December 31, 2019, we sold 475,024 shares of common stock under the sales agreement at an average price of approximately $12.57 per share for aggregate gross proceeds of approximately $6.0 million and net proceeds of approximately $5.8 million after deducting the sales commissions and offering expenses.

Cash Flows

The following table summarizes our sources and uses of cash for the years ended December 31, 2019 and 2018:

	Year Ended December 31,	
	2019	2018
Cash used in operating activities	$ (50,020)	$ (39,625)
Cash provided by (used in) investing activities	29,530	(83,156)
Cash provided by financing activities	16,140	69,523
Net increase (decrease) in cash and cash equivalents	$ (4,350)	$ (53,258)

Operating Activities

Net cash used in operating activities for the year ended December 31, 2019 was $50.0 million, primarily resulting from our net loss of $60.9 million, adjusted for net non-cash items of $3.8 million (primarily stock-based compensation and depreciation and amortization expense). Net cash provided by changes in our operating assets and liabilities was $7.2 million and consisted primarily of an increase of $14.2 million in accrued expenses and accounts payable and a $2.7 million decrease in prepaid expenses and other current assets, offset by a $7.1 million increase in receivables related to our government awards and a $2.9 million increase in other assets.

Net cash used in operating activities for the year ended December 31, 2018 was $39.6 million, primarily resulting from our net loss of $41.7 million, adjusted for net non-cash items of $3.1 million. Net cash used by changes in our operating assets and liabilities was $1.1 million and consisted primarily of a $5.5 million increase in prepaid expenses and other current assets as we prepare to initiate our pivotal Phase 3 trial for tebipenem HBr, a $1.2 million increase in other assets, and partially offset by a decrease of $1.4 million in receivables related to the Australian research and development tax incentive and to our government contracts, and an increase in accounts payable and accrued expenses and other current liabilities of $3.7 million.

Changes in accounts payable, accrued expenses and other current liabilities, and prepaid expenses and other current assets in all periods were generally due to growth in our business, the advancement of our development programs and the timing of vendor invoicing and payments.

Investing Activities

Net cash provided by investing activities for the year ended December 31, 2019 was $29.5 million and consisted primarily of the net maturities of marketable securities, as well as $0.3 million in property and equipment purchases. Cash used in investing activities during the year ended December 31, 2018 was $83.2 million and primarily related to the net purchase of marketable securities, as well as $2.4 million of fixed assets purchased, which included $1.6 million of fixed assets which will be used in manufacturing related activities at Meiji.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2019 was $16.1 million, consisting primarily of net proceeds of $5.8 million from the sale of common stock under our at-the-market offering program sales agreement, proceeds of $10.0 million from the sale of common stock to Novo, both of which were offset by offering expenses of $0.2 million, as well as $0.5 million of proceeds from the exercise of employee stock options.

Cash provided by financing activities during the year ended December 31, 2018, of $69.5 million primarily consisted of $69.5 million of net proceeds from our July 2018 equity offering (after deducting offering costs of $1.0 million), as well as $0.3 million of proceeds from the exercise of employee stock options, offset by $0.3 million of deferred offering costs related to our December 2018 registration statement and at-the-market facility.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials for our product candidates in development. In addition, we expect to incur additional costs associated with our continued operation as a public company. The timing and amount of our operating expenditures will depend largely on:

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

As of December 31, 2019, we had cash, cash equivalents and marketable securities of $82.0 million. In accordance with Accounting Standards Update ("ASU") 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40), we are required to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern from the issuance date of our financial statements. Based on our current plans, we believe that our existing cash, cash equivalents and marketable securities as of December 31, 2019, together with committed funding from our BARDA contract and other non-dilutive funding commitments, together with the net proceeds from our rights offering completed in early March 2020, will not be sufficient to fund our operating expenses and capital expenditure requirements, as currently planned, for more than one year beyond the filing date of this Annual Report on Form 10-K. Specifically, we believe these funds will enable us to fund our operating expenses and capital expenditure requirements into the first quarter of 2021, including through the filing of an NDA for tebipenem HBr. Because these funds will not be sufficient to fund our operations, as currently planned, for more than one year beyond the filing date of this Annual Report on Form 10-K, we have determined that there is substantial doubt regarding our ability to continue as a going concern. Our consolidated financial statements as of December 31, 2019 were prepared under the assumption that we will continue as a going concern for the next twelve months. As a result, the opinion from our independent registered public accounting firm with respect to our annual financial statements contains an explanatory paragraph about such substantial doubt about our ability to continue as a going concern. Our ability to continue as a going concern is dependent upon our ability to obtain additional equity or debt financing, attain further operating efficiencies, reduce expenditures, and, ultimately, to generate revenue. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. The substantial doubt about our ability to continue as a going concern may adversely affect our stock price and our ability to raise capital. There is no assurance that we will be successful in obtaining sufficient funding on acceptable terms, if at all, and we could be forced to delay, reduce or eliminate some or all of our research and development programs, product portfolio expansion or commercialization efforts, which could materially adversely affect our business prospects or our ability to continue operations.

We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical product candidates, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements will depend on and could increase significantly as a result of many factors, including those listed above.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of equity offerings, debt financings, government funding, collaborations, strategic alliances and marketing, distribution or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. 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 acquisitions or 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 have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our research, product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

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

	Payments Due by Period				
	Total	Less Than 1 Year	1 to 3 Years	4 to 5 Years	More than 5 Years
	(in thousands)				
Operating lease commitments (1)	7,886	1,361	2,049	2,230	2,246
Total	$ 7,886	$ 1,361	$ 2,049	$ 2,230	$ 2,246

(1) Reflects payments due for our lease of office space under an operating lease agreement that expires in 2027. Total minimum future lease payments of approximately $4.3 million for a lease that has not commenced as of December 31, 2019 is not included in the table above or in the lease liability in the consolidated financial statements, as the Company does not yet have control of the underlying asset. The lease is expected to commence in June 2020 with a lease term of 7 years.

As further described below, under various licensing and related agreements with third parties, we have agreed to make milestone payments and pay royalties to third parties. We have not included any contingent payment obligations, such as milestones or royalties, in the table above as the amount, timing and likelihood of such payments are not known.

Under our license agreement with Meiji, we are obligated (i) to make milestone payments of up to $3.0 million upon the achievement of specified clinical and regulatory milestones, (ii) to pay royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement and (iii) to pay to Meiji a low double-digit percentage of any sublicense fees received by us up to $7.5 million. During the fourth quarter of 2018 we paid Meiji approximately $1.6 million related to fixed assets which will be used in manufacturing related activities at Meiji. The equipment has been capitalized as property and equipment in the consolidated balance sheet as of December 31, 2018 and 2019.

Under an agreement we entered into with PBB, we are obligated to make milestone payments of up to $5.8 million upon the achievement of specified clinical milestones and a payment of £5.0 million ($6.6 million as of December 31, 2019) upon the achievement of a specified commercial milestone. In addition, we have agreed to pay to PBB royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement. During the three months ended December 31, 2018, we recorded $0.2 million in expense related to the achievement of regulatory milestones for SPR206.

Under our agreement with Vertex, we are obligated to make milestone payments of up to $81.1 million upon the achievement of specified clinical, regulatory and commercial milestones and to pay to Vertex tiered royalties, on a product-by-product and country-by-country basis, of a mid single-digit to low double-digit percentage based on net sales of products licensed under the agreement. During the three months ended December 31, 2018, we recorded $0.2 million in expense related to the achievement of regulatory milestones for SPR720.

We enter into contracts in the normal course of business with CROs, CMOs and other third parties for clinical trials, preclinical research studies and testing, manufacturing and other services. These contracts are cancelable by us upon prior notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including non-cancellable obligations of our service providers, up to the date of cancellation. These payments are not included in the table of contractual obligations and commitments above.

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.

Recently Adopted Accounting Pronouncements

Please refer to Note 2 to our consolidated financial statements included in Part II, Item 8, “Financial Statements and Supplementary Data,” of this Annual Report on Form 10-K for a description of recent accounting pronouncements applicable to our business.

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

As of December 31, 2019, we had cash, cash equivalents and marketable securities of $82.0 million, consisting of cash, money market accounts, corporate bonds, commercial paper and U.S. government debt securities. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. If market interest rates were to increase immediately and uniformly by 50 basis points, from levels as of December 31, 2019, the net fair value of our interest sensitive marketable securities would hypothetically decline by less than $0.1 million. As we incur research expenses in foreign countries, we face exposure to movements in foreign currency exchange rates, primarily the Euro, British Pound and Australian dollar against the U.S. dollar. Historically, foreign currency fluctuations have not had a material impact on our consolidated financial statements.

Item 8. Financial Statements and Supplementary Data.

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Spero Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Spero Therapeutics, Inc. and its subsidiaries (the "Company") as of December 31, 2019 and 2018, and the related consolidated statements of operations and comprehensive loss, of convertible preferred shares and stockholders' equity and of cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Substantial Doubt About the Company's Ability to Continue as a Going Concern

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

Change in Accounting Principle

As discussed in Note 2 to the consolidated financial statements, the Company changed the manner in which it accounts for leases in 2019.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's 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 of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits 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/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 16, 2020

We have served as the Company's auditor since 2016.

SPERO THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS
(In thousands, except unit, share and per share amounts)

	December 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 29,730	$ 34,080
Marketable securities	52,315	81,363
Other receivables	7,760	376
Tax incentive receivable, current	786	922
Prepaid expenses and other current assets	4,823	7,478
Total current assets	95,414	124,219
Property and equipment, net	2,273	2,893
Tax incentive receivable	21	233
Operating lease right of use assets	4,875	—
Other assets	3,520	1,661
Total assets	$ 106,103	$ 129,006
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 4,147	$ 3,603
Accrued expenses and other current liabilities	21,588	8,263
Derivative liabilities	—	223
Deferred rent	—	229
Operating lease liabilities	928	—
Total current liabilities	26,663	12,318
Deferred rent, net of current portion	—	833
Non-current operating lease liabilities	4,617	—
Other long-term liabilities	249	—
Total liabilities	31,529	13,151
Commitments and contingencies (Note 12)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized, 2,720 shares issued and outstanding as of December 31, 2019 and 3,220 shares issued and outstanding as of December 31, 2018	—	—
Common stock, $0.001 par value; 60,000,000 shares authorized as of December 31, 2019 and December 31, 2018;19,190,695 shares issued and outstanding as of December 31, 2019 and 17,205,962 shares issued and outstanding as of December 31, 2018	19	17
Additional paid-in capital	273,966	254,013
Accumulated deficit	(199,427)	(138,502)
Accumulated other comprehensive gain (loss)	16	(28)
Total Spero Therapeutics, Inc. stockholders' equity	74,574	115,500
Non-controlling interests	—	355
Total stockholders' equity	74,574	115,855
Total liabilities and stockholders' equity	$ 106,103	$ 129,006

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

SPERO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share data)

	Year Ended December 31,	
	2019	2018
Revenues:		
Grant revenue	$ 13,405	$ 3,966
Collaboration revenue	4,742	—
Total revenues	18,147	3,966
Operating expenses:		
Research and development	65,775	33,885
General and administrative	15,588	12,887
Total operating expenses	81,363	46,772
Loss from operations	(63,216)	(42,806)
Other income (expense):		
Gain on settlement of derivative liability	223	—
Interest income	1,328	1,101
Other income (expense), net	740	43
Total other income (expense), net	2,291	1,144
Net loss	$ (60,925)	$ (41,662)
Net loss per share attributable to common stockholders, basic and diluted	$ (3.35)	$ (2.60)
Weighted average common shares outstanding, basic and diluted:	18,160,525	16,001,832
Comprehensive loss:		
Net loss	(60,925)	(41,662)
Other comprehensive gain (loss):		
Unrealized gain (loss) on marketable securities	38	(28)
Reclassification adjustment for gains included in net loss	6	—
Net unrealized gains (losses) on securities	44	(28)
Total comprehensive loss	$ (60,881)	$ (41,690)

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

SPERO THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED SHARES AND STOCKHOLDERS' EQUITY
(In thousands, except unit and share amounts)

	Series A and B Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Accumulated Other Comprehensive	Spero Therapeutics, Inc. Stockholders'	Non-controlling	Total Stockholders'
	Shares	Par Value	Shares	Par Value	Capital	Deficit	Income (Loss)	Equity (Deficit)	Interests	Equity
Balances at December 31, 2017	—	$ —	14,369,182	14	181,428	$ (96,840)	$ —	$ 84,602	$ 355	$ 84,957
Issuance of common stock upon the exercise of stock options	—	—	56,780	—	335	—	—	335	—	335
Issuance of common and Series A preferred stock in public offering, net of issuance costs of $996	2,220	—	3,780,000	4	69,500	—	—	69,504	—	69,504
Issuance of Series B preferred stock in exchange for common stock	1,000	—	(1,000,000)	(1)	1	—	—	—	—	—
Share-based compensation expense	—	—	—	—	2,749	—	—	2,749	—	2,749
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	(28)	(28)	—	(28)
Net loss	—	—	—	—	—	(41,662)	—	(41,662)	—	(41,662)
Balances at December 31, 2018	3,220	—	17,205,962	17	254,013	(138,502)	(28)	115,500	355	115,855
Issuance of common stock upon the exercise of stock options	—	—	78,610	—	508	—	—	508	—	508
Issuance of common stock, net of issuance costs of $474	—	—	1,406,123	1	15,315	—	—	15,316	—	15,316
Conversion of convertible preferred stock to common stock	(500)	—	500,000	1	(1)	—	—	—		—
Share-based compensation expense	—	—	—	—	3,776	—	—	3,776	—	3,776
Purchase of non-controlling interest in Spero Gyrase, Inc.	—	—	—	—	355	—	—	355	(355)	—
Unrealized gain on available-for-sale securities	—	—	—	—	—	—	44	44	—	44
Net loss	—	—	—	—	—	(60,925)	—	(60,925)	—	(60,925)
Balances at December 31, 2019	2,720	—	19,190,695	19	273,966	(199,427)	16	74,574	—	74,574

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

SPERO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,	
	2019	**2018**
Cash flows from operating activities:		
Net loss	$ (60,925)	$ (41,662)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	750	409
Non-cash lease cost	408	—
Loss on disposal of fixed assets	184	248
Gain on settlement of derivative liability	(223)	—
Share-based compensation	3,776	2,749
Realized (gain) loss on investments	(1)	—
Unrealized foreign currency transaction (gain) loss	(18)	373
Accretion of discount on marketable securities	(750)	(671)
Changes in operating assets and liabilities:		
Other receivables	(7,384)	635
Prepaid expenses and other current assets	2,654	(5,497)
Tax incentive receivables	299	770
Other assets	(2,912)	(1,192)
Accounts payable	564	84
Accrued expenses and other current liabilities	13,610	3,575
Deferred rent	—	554
Other long-term liabilities	(52)	—
Net cash used in operating activities	(50,020)	(39,625)
Cash flows from investing activities:		
Purchases of marketable securities	(88,993)	(130,175)
Proceeds from maturities of marketable securities	118,837	49,455
Purchases of property and equipment	(314)	(2,436)
Net cash provided by (used in) investing activities	29,530	(83,156)
Cash flows from financing activities:		
Proceeds from the issuance of common stock, net of commissions	15,790	—
Payment of offering costs related to 2018 registration statement and at-the-market-facility	(158)	(316)
Proceeds from 2018 equity offering	—	70,500
Payment of offering costs related to 2018 equity offering	—	(996)
Proceeds from stock option exercises	508	335
Net cash provided by financing activities	16,140	69,523
Net increase (decrease) in cash and cash equivalents	(4,350)	(53,258)
Cash, cash equivalents and restricted cash at beginning of period	34,080	87,338
Cash, cash equivalents and restricted cash at end of period	$ 29,730	$ 34,080
Supplemental disclosure of non-cash investing and financing activities:		
Purchases of property and equipment included in accounts payable and accrued expenses	$ —	$ 54

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

1. Nature of the Business and Basis of Presentation

Spero Therapeutics, Inc., together with its consolidated subsidiaries (the "Company" or "Spero"), is a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing and commercializing treatments in high unmet need areas involving multi-drug resistant ("MDR") bacterial infections. The Company's most advanced product candidate, tebipenem HBr, is designed to be the first broad-spectrum oral carbapenem-class antibiotic for use in adults to treat MDR Gram-negative infections. Treatment with effective orally administrable antibiotics may prevent hospitalizations for serious infections and enable earlier, more convenient and cost-effective treatment of patients after hospitalization. The Company is also developing SPR720, a novel oral antibiotic designed for the treatment of non-tuberculous mycobacterial ("NTM") disease, a rare, orphan disease caused by pulmonary non-tuberculous mycobacterial infections. In addition, the Company also has a platform technology known as its Potentiator Platform that includes an intravenous, or IV, administered product candidate, SPR206, which is being developed to treat MDR Gram-negative infections in the hospital.

The Company was formed as Spero Therapeutics, LLC in December 2013 under the laws of the State of Delaware. On June 30, 2017, through a series of transactions, Spero Therapeutics, LLC merged with and into Spero Therapeutics, Inc. (formerly known as Spero OpCo, Inc.), a Delaware corporation. As part of the transactions, holders of preferred units and common units of Spero Therapeutics, LLC exchanged their units for shares of Spero Therapeutics, Inc. on a one-for-one basis. These transactions are collectively referred to as the Reorganization. Upon completion of the Reorganization, the historical consolidated financial statements of Spero Therapeutics, LLC became the historical consolidated financial statements of Spero Therapeutics, Inc. because the Reorganization was accounted for as a reorganization of entities under common control.

On December 3, 2018, the Company filed a universal shelf registration statement on Form S-3 (Registration No. 333-228661) with the SEC, which was declared effective on December 11, 2018, and pursuant to which it registered for sale up to $200.0 million of any combination of its common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that we may determine, including up to $50.0 million of our common stock available for issuance pursuant to an at-the-market offering program sales agreement that it entered into with Cantor Fitzgerald & Co., or Cantor. Under the sales agreement, Cantor may sell the shares by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415 of the Securities Act.

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

In accordance with Accounting Standards Update ("ASU") 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued. Based on the Company's current operating plan and existing cash, cash equivalents and market securities, the Company has determined that there is substantial doubt regarding its ability to continue as a going concern. The Company will require additional funding to fund the development of its product candidates through regulatory approval and commercialization, and to support its continued operations. The Company will seek additional funding through public or private financings, debt financing, collaboration agreements or government grants. There is no assurance that the Company will be successful in obtaining sufficient funding on acceptable terms, if at all, and it could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could materially adversely affect its business prospects or its ability to continue operations.

Since inception, the Company has funded its operations with proceeds from sales of preferred units (including bridge units, which converted into preferred units), payments received in connection with a concluded collaboration agreement and funding from government contracts, and most recently, with proceeds from the Company's initial public offering ("IPO") completed in November 2017. The Company has incurred recurring losses since inception, including net losses attributable to Spero Therapeutics, Inc. of $60.9 million and $41.7 million for the years ended December 31, 2019 and 2018, respectively. In addition, as of December 31, 2019, the Company had an accumulated deficit of $199.4 million. The Company expects to continue to generate operating losses for the foreseeable future.

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

2. Summary of Significant Accounting Policies

Use of Estimates

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

Consolidation

The Company consolidates entities in which it has a controlling financial interest. The Company evaluates each of its subsidiaries to determine whether the entity represents a variable interest entity ("VIE"), for which consolidation should be evaluated under the VIE model, or, alternatively, if the entity is a voting interest entity, for which consolidation should be evaluated using the voting interest model. The Company has concluded that none of its subsidiaries is a VIE and has consolidated each subsidiary under the voting interest model because it has majority voting control of each subsidiary.

Ownership interests in the Company's subsidiaries that are held by entities other than the Company are reported as non-controlling interests in the consolidated balance sheets. Losses attributed to non-controlling interests and to the Company are reported separately in the consolidated statements of operations and comprehensive loss.

As of December 31, 2018, the Company consolidated its non-controlling interest in Spero Gyrase, Inc. In December 2019, the Company repurchased 100% of the minority investor's outstanding shares in Spero Gyrase, Inc. for $0.001 per share, and as a result, as of December 31, 2019, the Company no longer reported a non-controlling interest.

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 cash equivalents. The Company maintains most of its cash and cash equivalents at one accredited financial institution. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on third-party manufacturers to supply products for research and development activities in its programs. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders' deficit as a reduction of additional paid-in capital generated as a result of the offering. Should the planned equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss.

Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents.

Marketable Securities

Marketable securities consist of investments with original maturities greater than 90 days. The Company considers its investment portfolio to be available-for-sale. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Investments with maturities beyond one year are generally classified as short-term, based on their highly liquid nature and because such marketable securities represent the investment of cash that is available for current operations. Unrealized gains and losses are reported as a component of accumulated other comprehensive income (loss) in stockholders' equity. Realized gains and losses and declines in value judged to be other than temporary are included as a component of other income (expense), net based on the specific identification method. When determining whether a decline in value is other than temporary, the Company considers various factors, including whether the Company has the intent to sell the security, and whether it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis.

Property and Equipment

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

	Estimated Useful Life
Laboratory equipment	5 years
Computer software and equipment	3 years
Office furniture and equipment	7 years
Manufacturing equipment	5 years
Leasehold improvements	Shorter of life of lease or 5 years

Costs for capital assets not yet placed into service are capitalized as construction in progress and are depreciated in accordance with the above guidelines once placed into service. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance are charged to expense as incurred.

Leases

Effective January 1, 2019, the Company adopted ASC Topic 842, *Leases* ("ASC 842"), using the modified retrospective approach and utilizing the effective date as its date of initial application, for which prior periods are presented in accordance with the previous guidance in ASC 840, *Leases ("ASC 840").*

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company has elected not to recognize on the balance sheet leases with terms of one year or less. As of December 31, 2019, the Company's short term leases with terms of one year or less were not material. Options to renew a lease are not included in the Company's initial lease term assessment unless there is reasonable certainty that the Company will renew. The Company monitors its plans to renew its material leases on a quarterly basis.

Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate ("IBR"), which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, and in a similar economic environment. Since the Company does not have any debt and has not been rated by any major credit rating agency, the Company's IBR was estimated by developing a synthetic credit rating for the Company. In transitioning to ASC 842, the Company utilized the remaining lease term of its leases in determining the appropriate incremental borrowing rates.

In accordance with ASC 842, components of a lease should be split into three categories: lease components (e.g., land, building, etc.), non-lease components (e.g., common area maintenance, consumables, etc.), and non-components (e.g., property taxes, insurance, etc.). The fixed and in-substance fixed contract consideration (including any consideration related to non-components) must be allocated based on the respective relative fair values to the lease components and non-lease components.

Although separation of lease and non-lease components is required, certain practical expedients are available. Entities may elect the practical expedient to not separate lease and non-lease components. In making this election, entities would account for each lease component and the related non-lease component together as a single component. For new and amended leases beginning in 2019 and after, the Company has elected to account for the lease and non-lease components together as a single lease component.

Other Assets

Other assets consist of long-term prepayments and deposits.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group 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 group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows.

Fair Value Measurements

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

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

The Company’s cash equivalents and derivative liabilities are carried at fair value, determined according to the fair value hierarchy described above (see Note 3). The carrying values of the Company’s accounts payable and accrued expenses approximate their fair values due to the short-term nature of these liabilities.

Derivative Liabilities

In connection with certain equity financings, licensing transactions and research collaborations, the Company has identified certain embedded and freestanding derivatives, which are recorded as liabilities on the Company’s consolidated balance sheet and are remeasured to fair value at each reporting date until the derivative is settled. Changes in the fair value of the derivative liabilities are recognized as other income (expense) in the consolidated statement of operations and comprehensive loss.

Segment Information

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company’s singular focus is on identifying, developing and commercializing novel treatments for MDR bacterial infections. All of the Company’s tangible assets are held in the United States.

Collaboration Agreements

For collaboration agreements with a third party, to determine the appropriate statement of operations classification of the recognized funding, the Company first assesses whether the collaboration arrangement is within the scope of the accounting guidance for collaboration arrangements. If it is, the Company evaluates the collaborative arrangement for proper classification in the statement of operations based on the nature of the underlying activity and the Company assesses the payments to and from the collaborative partner. If the payments to and from the collaborative partner are not within the scope of other authoritative accounting guidance, the Company bases the statement of operations classification for the payments received on a reasonable, rational analogy to authoritative accounting guidance, applied in a consistent manner. Conversely, if the collaboration arrangement is not within the scope of accounting guidance for collaboration arrangements, the Company assesses whether the collaboration arrangement represents a vendor/customer relationship. If the collaborative arrangement does not represent a vendor/customer relationship, the Company then classifies the funding payments received in the statement of operations and comprehensive loss as a reduction of the related expense that is incurred.

In June 2019, the Company entered into a collaboration agreement with the Bill and Melinda Gates Medical Research Institute (the “Gates MRI”) and concluded that the agreement is within the scope of the accounting guidance for collaboration arrangements (see Note 14). Due to the cost-funded nature of the payments and the Company’s assessment that it does not have a vendor/customer relationship with the Gates MRI, the Company will recognize the funding received under the agreement as a reduction to the research and development expenses incurred, as the related expenses are incurred.

Government Tax Incentives

For available government tax incentives that the Company may earn without regard to the existence of taxable income and that require the Company to forego tax deductions or the use of future tax credits and net operating loss carryforwards, the Company classifies the funding recognized as a reduction of the related qualifying research and development expenses incurred.

Since the fourth quarter of 2016, the Company’s operating subsidiary in Australia has met the eligibility requirements to receive a 43.5% tax incentive for qualifying research and development activities (see Note 15). The Company recognizes these incentives as a reduction of research and development expenses in the consolidated statements of operations and comprehensive loss in the same period that the related qualifying expenses are incurred. Reductions of research and development expense recognized upon incurring qualifying expenses in advance of receipt of tax incentive payments are recorded in the consolidated balance sheet as tax incentive receivables.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities, including personnel salaries, share-based compensation and benefits, allocated facilities costs, depreciation, manufacturing expenses, costs related to the Company’s government contract and grant arrangements, and external costs of outside vendors engaged to conduct preclinical development activities, clinical trials as well as the cost of licensing technology. Upfront payments and milestone payments made for the licensing of technology are expensed as research and development in the period in which they are incurred. Advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed.

Clinical Trial and other Research Contract Costs and Accruals

The Company has entered into various research and development contracts with clinical research organizations and other companies both inside and outside of the United States. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. There may be instances in which payments made to these vendors exceed the level of service provided and will result in a prepayment of the expense. The Company records accruals for estimated ongoing research and clinical trial costs based on the services received and efforts expended pursuant to multiple contracts with these vendors. When evaluating the adequacy of the accrued liabilities, the Company analyzes the progress of the studies or trials, 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

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

Share-Based Compensation

The Company measures all share-based awards granted to employees and directors based on the fair value on the date of grant using the Black-Scholes option-pricing model. Compensation expense of those awards is recognized over the requisite service period, which is generally the vesting period of the respective award. The Company has historically issued awards with only service-based vesting conditions. In March 2019, the Company also granted awards with vesting tied to certain performance conditions. The Company records the expense for awards with service-based conditions using the straight-line method over the requisite service period, net of any actual forfeitures. The Company classifies share-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with shareholders. For the years ended December 31, 2019 and 2018, these changes related to unrealized gains and losses on the Company's available-for-sale marketable securities. There were no reclassifications out of comprehensive loss for the year ended December 31, 2018.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood 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.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases* (Topic 842) ("ASU 2016-02"), which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e., lessees and lessors), and will replace the existing guidance in ASC840, Leases. The FASB subsequently issued amendments to ASU 2016-02, which have the same effective date and transition date of January 1, 2019: (i) ASU No. 2018-10, Codification Improvements to Topic 842, Leases, which amends certain narrow aspects of the guidance issued in ASU 2016-02; and (ii) ASU 2018-11, Leases (Topic 842): Targeted Improvements, which allows for a transition approach to initially apply ASU 2016-02 at the adoption date and recognize a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption as well as an additional practical expedient for lessors to not separate non-lease components from the associated lease component. ASU 2016-02 requires lessees to classify leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use, or ROU, asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases under ASC 840. The guidance is effective for public entities for annual reporting periods beginning after December 15, 2018 and for interim periods within those fiscal years, and early adoption is permitted.

The Company elected to adopt ASU 2016-02 effective January 1, 2019 using the modified retrospective approach with no restatement of prior periods. This standard provides a number of optional practical expedients in transition. The Company applied the package of practical expedients to leases that commenced prior to the effective date whereby it elected to not reassess the following: (i) whether any expired or existing contracts contain leases; (ii) the lease classification for any expired or existing leases; and (iii) initial direct costs for any existing leases. The Company elected the short-term lease recognition exemption for all leases that qualified, and a right-of-use asset or lease liability was not recognized for short term leases.

The adoption of ASU 2016-02 resulted in the recognition of operating lease liabilities of $5.2 million and right-of-use assets of $6.1 million on the Company's condensed consolidated balance sheet as of January 1, 2019. These and corresponding liabilities relate to existing facility operating leases and an embedded financing lease for manufacturing equipment. Other than the recognition of these right-of-use assets and liabilities, the adoption of ASU 2016-02 did not have a material impact on the Company's consolidated statements of operations and comprehensive loss or consolidated statements of cash flows. No cumulative effect adjustment was recognized upon transition.

In July 2017, the FASB issued ASU 2017-11, *Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480), Derivatives and Hedging (Topic 815) I. Accounting for Certain Financial Instruments with Down Round Features II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception*. Part I applies to entities that issue financial instruments such as warrants, convertible debt or convertible preferred stock that contain down-round features. Part II replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within ASC Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. ASU 2017-11 is required to be adopted for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. The Company adopted the ASU effective January 1, 2019. The adoption of ASU 2017-11 did not have a material impact on the Company's consolidated financial statements.

In June 2018, the FASB issued ASU 2018-07, *Improvements to Nonemployee Share-Based Payment Accounting*, which sets forth amendments to simplify the accounting for share-based payment awards to nonemployees by aligning the measurement and classification guidance, with certain exceptions, to that for share-based payment awards to employees. The amendments expand the scope of the accounting standard for share-based payment awards to include share-based payment awards granted to non-employees in exchange for goods or services used or consumed in an entity's own operations and supersedes the guidance related to equity-based payments to non-employees. The amendments in this ASU are effective for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. The adoption of this standard did not have a material impact to its consolidated statement of operations, as awards to non-employees are not material.

3. Fair Value of Financial Assets and Liabilities

The following tables present information about the Company's assets and liabilities that are measured at fair value on a recurring basis (in thousands):

	Fair Value Measurements at December 31, 2019 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds		$ 26,751		$ 26,751
Commercial paper		—		—
Total cash equivalents	—	26,751	—	26,751
Marketable securities:				
U.S. government securities	—	16,797	—	16,797
Corporate bonds	—	14,060	—	14,060
Commercial paper	—	21,458	—	21,458
Total marketable securities	—	52,315	—	52,315
Total cash equivalents and marketable securities	$ —	$ 79,066	$ —	$ 79,066

	Fair Value Measurements at December 31, 2018 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ —	$ 22,327	$ —	$ 22,327
Commercial paper	—	6,389	—	6,389
Total cash equivalents	—	28,716	—	28,716
Marketable securities:				
U.S. government securities	—	37,815	—	37,815
Corporate bonds	—	26,672	—	26,672
Commercial paper	—	16,876	—	16,876
Total marketable securities	—	81,363	—	81,363
Total cash equivalents and marketable securities	$ —	$ 110,079	$ —	$ 110,079
Liabilities:				
Derivative liabilities:				
Anti-dilution rights	$ —	$ —	$ 223	$ 223
	$ —	$ —	$ 223	$ 223

The tables above do not include cash of $3.0 million and $5.4 million as of December 31, 2019 and 2018, respectively. During the years ended December 31, 2019 and 2018, there were no transfers between Level 1, Level 2 and Level 3.

Marketable Securities

The Company's marketable securities are classified as Level 2 assets under the fair value hierarchy as these assets were primarily determined from independent pricing sources, which generally derive security prices from recently reported trades for identical or similar securities.

The following table summarizes the gross unrealized gains and losses of the Company's marketable securities as of December 31, 2019 (in thousands):

	December 31, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets:				
U.S. government securities	$ 16,791	$ 6	$ —	$ 16,797
Corporate bonds	14,050	12	(2)	14,060
Commercial paper	21,458	—	—	21,458
	$ 52,299	$ 18	$ (2)	$ 52,315

As of December 31, 2019 and 2018, all of the Company's marketable securities had remaining contractual maturity dates of one year or less from the consolidated balance sheet date.

Anti-Dilution Rights

In connection with the issuance of non-controlling interests in certain of the Company's subsidiaries (see Note 10), specifically Spero Gyrase, Inc., the Company granted anti-dilution rights to the minority investors. The Company classified the anti-dilution rights as a derivative liability on its consolidated balance sheet because they were freestanding instruments that represent a conditional obligation to issue a variable number of shares. The Company remeasured the derivative liability associated with the anti-dilution rights to fair value at each reporting date, and recognized changes in the fair value of the derivative liability as a component of other income (expense) in the consolidated statement of operations and comprehensive loss. The fair value of these derivative liabilities was determined using a discounted cash flow model.

In March 2016, in connection with the issuance of a non-controlling interest in its subsidiary, Spero Gyrase, Inc. ("Spero Gyrase"), to Biota Pharmaceuticals, Inc. (now Vaxart, Inc.) ("Vaxart"), the Company granted to Vaxart certain anti-dilution rights (see Note 10). The fair value of the derivative liability related to the anti-dilution rights upon issuance in March 2016 was $1.6 million. During 2017, the fair value of the derivative liability decreased by $1.4 million to $0.2 million by June 30, 2017, representing the amounts funded to the entity that could be settled by the issuance of equity. In November 2019, the Company repurchased 100% of the minority investor's outstanding shares in Spero Gyrase, Inc. at a price per share of $0.001. As a result, as of December 31, 2019, there are no anti-dilution rights outstanding.

4. Property and Equipment, Net

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

	December 31,	
	2019	2018
Computer software and equipment	$ 438	$ 166
Office furniture and equipment	364	210
Leasehold improvements	1,636	863
Construction-in-progress	12	897
Manufacturing equipment	1,338	1,584
	3,788	3,720
Less: Accumulated depreciation and amortization	(1,515)	(827)
	$ 2,273	$ 2,893

Property and equipment additions during the year ended December 31, 2019 primarily related to leasehold improvements previously in construction-in-progress. Property and equipment additions during the year ended December 31, 2018, primarily related to leased manufacturing equipment which was fully paid by the Company, as well as construction-in-progress and leasehold improvements related to the expansion of Company's leased office space (see Note 5). Depreciation and amortization expense was $0.8 million and $0.4 million for the years ended December 31, 2019 and 2018, respectively. During the year ended December 31, 2019, the Company wrote off $0.2 million of leased manufacturing equipment which the Company determined did not have any further use. During the year ended December 31, 2018, the Company recorded a loss of $0.2 million related to the write-off of laboratory equipment and certain leasehold improvements at its Watertown, Massachusetts laboratory facility.

5. Leases

Operating Leases

In August 2015, the Company entered into an operating lease agreement with U.S. REIF Central Plaza Massachusetts, LLC (the "Landlord") with respect to its corporate headquarters located at 675 Massachusetts Avenue, Cambridge, Massachusetts (the "Original Lease"). The term of the Original Lease commenced in January 2016 and was scheduled to expire in December 2020. Under the terms of the Original Lease, the Company provided a security deposit of $0.2 million to the Landlord, which is included in long-term assets in the accompanying condensed consolidated balance sheets. The Original Lease provided for annual rent escalations as well as tenant incentives in the amount of $0.7 million, of which $0.3 million would be reimbursed to the Landlord over the initial term of the Original Lease. In determining its ROU assets as of January 1, 2019, the Company reduced the amount of ROU assets by $0.2 million, which was the remaining balance of lease incentives received from the Landlord as of that date. The lease does not include any restrictions or covenants that had to be accounted for under the lease guidance.

On January 17, 2018, the Company entered into an amendment to the Original Lease (the "Amendment"). The Amendment made certain modifications to the Original Lease, including the addition of approximately 7,800 square feet of office space in the same building and an extension of the expiration date of the Original Lease to seven years, or December 2025. The Amendment also provided for $0.4 million from the Landlord for leasehold improvements on the Expansion Premises. In determining its ROU assets as of January 1, 2019, the Company reduced the amount of ROU assets by $0.4 million, which was the remaining balance of lease incentives received from the Landlord as of that date. The lease does not include any restrictions or covenants that had to be accounted for under the lease guidance.

On December 16, 2019, the Company entered into a second amendment to the Original Lease and the Amendment (the "Second Amendment"). The Second Amendment made certain modifications, including (i) the addition of approximately 7,800 square feet of office space in the same building (the "Expansion Premises") with a term beginning on June 2020 and expiring on May 2027, and (ii) an extension of the expiration date of the lease through May 2027.

Under the Second Amendment, the Company has two consecutive options to extend the Lease Term for an additional period of five years (the "Option Terms"), subject to certain conditions, upon notice to the Landlord. These renewal options were not included in the calculation of the operating lease assets and operating lease liabilities, as the renewal is not reasonably certain. The Second Amendment provides for annual base rent for the Expansion Premises of approximately $0.6 million in the first year of the Lease Term, which increases on an annual basis to approximately $0.7 million in the final year of the Lease Term, and annual base rent during the Option Terms to be calculated based on the Landlord's good faith determination of 100% of the fair market rate for such Option Terms. The Company is also obligated to pay the Landlord certain costs, taxes and operating expenses, subject to certain exclusions. The Second Amendment also provides for $0.4 million from the Landlord for leasehold improvements on the Expansion Premises.

In July 2016, the Company entered into an agreement to lease laboratory space through November 30, 2019 from a sublessor, which required annual lease payments of $0.3 million, subject to certain escalations.

For the year ended December 31, 2019, the components of operating lease expense were as follows (in thousands):

Operating lease expense	Statement of Operations Location	December 31, 2019
Fixed operating lease expense	Research and development expense	601
	General and administrative expense	641
Variable operating lease expense	Research and development expense	56
	General and administrative expense	181
Total operating lease expense		$ 1,479

Supplemental cash flow information related to the Company's operating leases for the year ended December 31, 2019, was as follows (in thousands):

	December 31, 2019
Cash paid for amounts included in the measurement of lease liabilities:	
Operating cash flows from operating leases	$ 1,234
Non cash amounts resulting from the measurement of the lease liabilities:	
Right of use asset and lease obligation recorded upon amendment of lease agreements	$ 1,038

Embedded Finance Leases

As part of our agreement with Meiji Seika Pharma Co. Ltd. ("Meiji"), the Company paid Meiji approximately $1.6 million during the three months ended December 31, 2018, related to fixed assets which will be used in manufacturing related activities at Meiji. The Company determined this equipment to be an embedded finance lease and has been capitalized as property and equipment in the condensed consolidated balance sheet as of December 31, 2019 and 2018. As this equipment was fully paid in 2018, there is no corresponding lease liability as of December 31, 2019.

The following table presents the lease balances within the condensed consolidated balance sheet, weighted average remaining lease term, and the weighted average discount rates related to the Company's operating and finance leases as of December 31, 2019 (in thousands, except for the weighted average remaining lease term, which is in years, and the weighted average discount rate):

Lease Assets and Liabilities	Classification	December 31, 2019
Assets		
Operating	Operating lease right of use assets	$ 4,875
Financing	Property and equipment, net	1,004
Total leased assets		$ 5,879
Liabilities		
Current		
Operating	Operating lease liabilities	$ 928
Non-Current		
Operating	Non-current operating lease liabilities	4,617
Total lease liabilities		$ 5,545
Weighted average remaining lease term		7
Weighted average discount rate		10%

The following table presents the maturity of the Company's operating lease liabilities as of December 31, 2019 (in thousands):

Years Ending December 31,	
2020	$ 928
2021	943
2022	1,061
2023	1,076
2024	1,092
Thereafter	2,969
Total future minimum lease payments	8,069
Less imputed interest	(2,524)
Total operating lease liabilities	$ 5,545

The following table summarizes the future minimum payments due for the Company's operating leases under the prior lease guidance for each of the next five years and total thereafter as of December 31, 2018 (in thousands):

Years Ending December 31,	
2019	$ 1,361
2020	1,054
2021	995
2022	1,107
2023	1,123
Thereafter	2,246
	$ 7,886

Total minimum future lease payments of approximately $4.3 million for a lease that has not commenced as of December 31, 2019 is not included in the table above or in the lease liability in consolidated financial statements, as the Company does not yet have control of the underlying asset. The lease is expected to commence in June 2020 with a lease term of 7 years.

Rent expense during the year ended December 31, 2018 was $0.8 million.

6. Accrued Expenses and Other Current Liabilities

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

	December 31, 2019	December 31, 2018
Accrued external research and development expenses	$ 17,746	$ 4,541
Accrued payroll and related expenses	2,630	2,379
Accrued professional fees	803	917
Accrued other	409	426
	$ 21,588	$ 8,263

7. Convertible Preferred Shares

Series A Convertible Preferred Shares

The Company's amended and restated certificate of incorporation authorizes its Board of Directors to issue up to 10,000,000 shares of preferred stock, par value $0.001 per share. As part of the Company's July 2018 underwritten public offering, 2,220 shares were designated as Series A Convertible Preferred Stock and issued at a price of $12,500 per share.

Each share of Series A Convertible Preferred Stock is convertible into 1,000 shares of the Company's common stock at any time at the option of the holder, provided that the holder will be prohibited from converting the Series A Convertible Preferred Stock into shares of common stock if, as a result of such conversion, the holder, together with its affiliates, would own more than 9.99% of the total number of shares of the Company's common stock then issued and outstanding. In the event of the Company's liquidation, dissolution, or winding up, holders of Series A Convertible Preferred Stock will receive a payment equal to $0.001 per share of Series A Convertible Preferred Stock, plus an additional amount equal to any dividends declared but unpaid on such shares, before any proceeds are distributed to the holders of common stock or any of our securities that by their terms are junior to the Series A Convertible Preferred Stock. The Series A Convertible Preferred Stock has no voting rights, except as required by law and except that the consent of the outstanding Series A Convertible Preferred Stock holders will be required to amend the terms of the Series A Convertible Preferred Stock. The Series A Convertible Preferred Stock does not have any mandatory redemption rights or other redemption rights that would be outside of the Company's control. As such, the Company has classified the Series A Convertible Preferred Stock within permanent equity in its consolidated balance sheet.

Series B Convertible Preferred Shares

On November 15, 2018, the Company and Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., Biotechnology Value Trading Fund OS, L.P. and MSI BVF SPV LLC (collectively, "BVF") entered into an Exchange Agreement (the "Exchange Agreement") pursuant to which BVF agreed to exchange (the "Exchange") an aggregate of 1,000,000 shares of the Company's common stock, par value $0.001, owned by BVF for an aggregate of 1,000 shares of the Company's newly designated Series B Convertible Preferred Stock, par value $0.001 per share. On November 16, 2018, as part of this exchange, 1,000 shares of the Company's authorized and unissued preferred stock were designated as Series B Convertible Preferred Stock and issued at a price of $7,950 per share. The Series B Preferred Stock has substantially the same terms as the Company's Series A Convertible Preferred Stock.

Each share of Series B Preferred Stock is convertible into 1,000 shares of Common Stock at any time at the option of the holder, provided that the holder will be prohibited from converting the Series B Preferred Stock into shares of Common Stock if, as a result of such conversion, the holder, together with its affiliates, would own more than 9.99% of the total number of shares of Common Stock then issued and outstanding, subject to certain exceptions. In the event of the Company's liquidation, dissolution, or winding up, holders of Series B Preferred Stock will receive a payment equal to $0.001 per share of Series B Preferred Stock before any proceeds are distributed to the holders of Common Stock and equal to any distributions to the holders of the Series A Convertible Preferred Stock. The Series B Convertible Preferred Stock does not have any mandatory redemption rights or other redemption rights that would be outside of the Company's control. As such, the Company has classified the Series B Convertible Preferred Stock within permanent equity in its consolidated balance sheet.

8. Common Stock

On July 17, 2018, the Company completed an underwritten public offering of its common and preferred stock, which resulted in the sale of 3,780,000 shares of common stock at a price of $12.50 per share, and 2,220 shares of Series A Convertible Preferred Stock at a price of $12,500 per share. Each share of Series A Convertible Preferred Stock sold in the offering is convertible into 1,000 shares of the Company's common stock. The Company received net proceeds from the offering of approximately $70.5 million after deducting underwriting discounts and commissions but before deducting $1.0 million of offering expenses payable by the Company.

On December 3, 2018, the Company filed a universal shelf registration statement on Form S-3 (Registration No. 333-228661) with the SEC, which was declared effective on December 11, 2018, and pursuant to which the Company registered for sale up to $200.0 million of any combination of its common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that it may determine, including up to $50.0 million of its common stock available for issuance pursuant to an at-the-market offering program sales agreement that it entered into with Cantor Fitzgerald & Co. Under the sales agreement, Cantor may sell shares of the Company's common stock by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415 of the Securities Act, subject to the terms of the sales agreement. During the year ended December 31, 2019, the Company sold 475,024 shares of its common stock under the sales agreement at an average price of approximately $12.57 per share for aggregate gross proceeds of approximately $6.0 million and net proceeds of approximately $5.8 million after deducting sales commissions. The Company incurred approximately $0.3 million of costs related to the shelf registration statement and at the market offering. These costs were classified as deferred offering costs on the Company's balance sheet as of December 31, 2018, and were charged to additional paid-in-capital during the year ended December 31, 2019 upon the issuance of the associated equity.

On June 12, 2019, the Company entered into a securities purchase agreement with Novo Holdings A/S ("Novo") to sell up to an aggregate of $10.0 million of its common stock, $0.001 par value per share, in two closings pursuant to the Company's effective registration statement on Form S-3 (Registration No. 333-228661). The initial closing occurred on June 14, 2019 and consisted of 465,983 shares of common stock sold at a price of $10.73 per share for gross proceeds of $5.0 million prior to deducting offering expenses. The second closing of approximately $5.0 million occurred on October 18, 2019, pursuant to the terms of the securities purchase agreement. The number of shares sold in the second closing was determined by the volume weighted average trading price ("VWAP") of the Company's common stock prior to the date of the second closing, and consisted of 465,116 shares of common stock sold at a price of $10.75 per share for gross proceeds of approximately $5.0 million prior to deducting offering expenses.

In June 2019, a holder of the Company's Series A Convertible Preferred stock elected to convert 500 shares into 500,000 shares of the Company's common stock, pursuant to such holder's rights under the certificate of designation for such Series A Convertible Preferred Stock.

9. Share-Based Compensation

Incentive Stock Units

Prior to the Reorganization, the Company's operating agreement, as amended and restated, provided for the granting of incentive units to officers, directors, employees, consultants and advisors. Under the terms of the incentive unit grant agreements, such incentive units were subject to a vesting schedule, with 25% of the incentive units vesting following one year of continued employment or service and the balance vesting in equal monthly installments for 36 months beginning on the one-year anniversary of the holder's employment or service with the Company. Holders of incentive units were entitled to receive distributions in proportion to their ownership percent interest, when and if distributed, that were in excess of the strike price of the award set by the board of directors on the date of grant. The Company determined that the underlying terms of the incentive units and the intended purpose of the awards were more akin to an equity-based compensation award than a performance bonus or profit-sharing arrangement and, therefore, the incentive units were equity-classified awards.

The total number of incentive units that could have been issued under the Company's operating agreement was 573,156 as of December 31, 2016, of which 159,890 units remained available for future issuance as of December 31, 2016. Upon the Reorganization on June 30, 2017 (see Note 1), the Company could no longer issue incentive units. In addition, in June 2017, in connection with the Reorganization, the Company cancelled the then-outstanding 402,857 incentive units. As of December 31, 2017, all of the incentive units were cancelled; however, the Company will continue to recognize compensation costs related to these awards (see below).

2017 Stock Incentive Plan

On June 28, 2017, the Company's stockholders approved the 2017 Stock Incentive Plan (the "2017 Plan"). The 2017 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock grants and stock-based awards. The 2017 Plan is administered by the board of directors, or at the discretion of the board of directors, by a committee of the board. The exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, or their committee if so delegated, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the share of common stock on the date of grant and the term of stock option may not be greater than ten years. The number of shares initially reserved for issuance under the 2017 Plan was 1,785,416 shares of common stock. The shares of common stock underlying any awards that are forfeited, cancelled, repurchased or are otherwise terminated by the Company under the 2017 Plan will be added back to the shares of common stock available for issuance under the 2017 Plan.

In July 2017, the Company additionally granted options for the purchase of 1,154,989 shares of common stock at an exercise price of $5.90 per share under the 2017 Plan. The options vest over four years and the fair value of these option grants was $3.96 per share.

In July 2017, previous holders of the cancelled incentive units who were still employed by the Company at the time of the Reorganization received stock options under the 2017 Stock Incentive Plan (described below). Such stock options were granted for the same number of shares of common stock as the number of incentive units cancelled, and the stock options were granted on the same vesting terms as the incentive units. All such stock options have an exercise price of $5.90 per share. The Company accounted for the cancellation of the incentive units and the issuance of new awards as a modification of the awards for accounting purposes in the three months ended September 30, 2017. Unrecognized compensation expense related to the original award is being recognized over the remaining service period of the modified award. The incremental fair value of the replacement options, based on the positive difference between the fair value of the modified award and the fair value of the original award immediately before it was modified was not material.

On October 18, 2017, the Company's stockholders approved an amendment to the 2017 Plan, which became effective upon the completion of the Company's IPO, to increase the total number of shares reserved for issuance under the 2017 Plan from 1,785,416 to 2,696,401. Additionally, the number of shares of common stock that may be issued under the 2017 Plan will automatically increase on each January 1, beginning with the fiscal year ending December 31, 2019 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2027, equal to the lowest of (i) 607,324 shares of common stock, (ii) 4% of the outstanding shares of common stock on such date and (iii) an amount determined by the Company's board of directors or compensation committee. As of December 31, 2019, there were 329,457 shares remaining available to be issued under the 2017 Plan.

2019 Equity Incentive Plan

On March 11, 2019, the Company adopted the 2019 Inducement Equity Incentive Plan (the "2019 Inducement Plan") to reserve 331,500 shares of its common stock to be used exclusively for grants of awards to individuals that were not previously employees or directors of the Company as a material inducement to such individuals' entry into employment with Spero within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. The terms and conditions of the 2019 Inducement Plan are substantially similar to those of the 2017 Plan. As of December 31, 2019, there were 160,200 shares remaining available to be issued under the 2019 Inducement Plan.

As of December 31, 2019, a total of 3,635,225 shares have been authorized and reserved for issuance under all equity plans and 489,657 shares were available for future issuance under such plans.

The following table summarizes stock option activity for all of our plans during 2019:

	2017 Plan	2019 Inducement Plan	Total Number of Stock Options
Outstanding as of December 31, 2018	2,297,810	—	2,297,810
Granted	870,434	171,300	1,041,734
Exercised	(78,610)	—	(78,610)
Forfeited or cancelled	(291,506)	—	(291,506)
Outstanding as of December 31, 2019	2,798,128	171,300	2,969,428

During 2019, the Company also granted 100,000 options and 50,000 restricted stock units ("RSUs") containing the same performance-based vesting criteria. The 100,000 options are included in the table above but the 50,000 RSU's are excluded from the table. These options and RSUs (the "Performance Awards") are subject to performance-based vesting eligibility and a subsequent partial time-based vesting schedule. Specifically, the Performance Awards are eligible for vesting based on the achievement of performance criteria, each representing a 25% vesting opportunity if achieved within a specified time during the performance period (the "Performance Period"), and relating to (i) the release of tebipenem HBr top-line data; (ii) FDA acceptance of a tebipenem HBr New Drug Application; (iii) non-dilutive financing; and (iv) equity financing. Following the Performance Period, Performance Awards determined to be eligible for vesting as a result of achievement of the performance criteria will vest as follows: (a) 50% of the eligible award will vest immediately, and (b) the remaining eligible award will vest (i) in the case of options, in equal monthly instalments ending two years after the Performance Period expiration, and (ii) in the case of RSUs, on such two year anniversary. No compensation expense was recognized in 2019 associated with performance-based awards as the performance condition is not yet probable of achievement. Recognition of stock-based compensation expense associated with these performance-based stock options and RSUs will commence when the performance condition is considered probable of achievement, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

Stock Option Valuation

The fair value of stock options is estimated using the Black-Scholes option-pricing model. The Company does not have sufficient company-specific historical and implied volatility information and it therefore estimates its expected share volatility based on the historical volatility of a set of publicly traded peer companies. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded share price. The Company has estimated the expected term of the Company's stock option awards utilizing the "simplified" method for awards that qualify as "plain-vanilla." 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. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

The assumptions that the Company used in the Black-Scholes option-pricing model to determine the fair value of stock option awards granted to employees and directors were as follows, presented on a weighted average basis:

	Year Ended December 31,	
	2019	2018
Risk-free interest rate	2.4%	2.7%
Expected term (in years)	6.3	6.3
Expected volatility	75.2%	74.1%
Expected dividend yield	0.0%	0.0%

The following table summarizes details regarding stock options granted under our equity incentive plans for the year ended December 31, 2019:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2018	2,297,810	$ 8.03	8.77	$ 354
Granted	1,041,734	8.25	—	—
Exercised	(78,610)	6.46	—	—
Forfeited or cancelled	(291,506)	8.21	—	—
Outstanding as of December 31, 2019	2,969,428	$ 8.13	7.94	$ 6,689
Outstanding as of December 31, 2019 - vested and expected to vest	2,969,428	$ 8.13	7.94	$ 6,689
Exercisable at December 31, 2019	1,339,002	$ 7.56	7.08	$ 3,566

The weighted average grant-date fair value of stock options granted during the year ended December 31, 2019 was $5.62 per share. The weighted average grant-date fair value of awards granted during the years ended December 31, 2018 was $7.63 per share. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2019 and 2018 was approximately $0.4 million and $0.3 million, respectively. The Company satisfies stock option exercises with newly issued shares of its common stock.

As of December 31, 2019, total unrecognized compensation cost related to unvested stock option grants was approximately $7.7 million. This amount is expected to be recognized over a weighted average period of approximately 2.5 years.

The Company recorded share-based compensation expense, for both incentive units and stock options in the following expense categories of its consolidated statements of operations and comprehensive loss (in thousands):

	Year Ended December 31,	
	2019	2018
Research and development expenses	$ 1,580	$ 1,072
General and administrative expenses	2,196	1,677
Total	$ 3,776	$ 2,749

10. Non-Controlling Interests

Spero Gyrase

In March 2016, the Company entered into an agreement with Aviragen and its affiliates in order to acquire certain intellectual property and know-how related to certain compounds. In connection with the transaction, the Company established Spero Gyrase, a Delaware corporation, and issued to Aviragen 200 common shares of Spero Gyrase with a fair value of $1.1 million, which represented a 20% equity ownership interest in Spero Gyrase. In addition, Spero Gyrase agreed to make future milestone and royalty payments in exchange for the intellectual property. The Company accounted for the acquisition of technology as an asset acquisition because it did not meet the definition of a business. The Company recorded the acquired technology as research and development expense in the consolidated statement of operations and comprehensive loss in the amount of $1.1 million, because the acquired technology had not reached commercial feasibility and had no alternative future use, and recorded a non-controlling interest in Spero Gyrase in a corresponding amount. In November 2019, the Company repurchased 100% of the minority investor's outstanding shares in Spero Gyrase, Inc. at a price per share of $0.001. As a result, as of December 31, 2019, the Company no longer reports a non-controlling interest.

As of December 31, 2018, the Company's only remaining non-controlling interest related to Spero Gyrase, Inc., which totaled $0.4 million.

11. Income Taxes

Prior to the Reorganization (see Note 1), the Company's former parent company, Spero Therapeutics, LLC, was treated as a partnership for federal income tax purposes and, therefore, its owners, and not itself, were subject to U.S. federal or state income taxation on the income of Spero Therapeutics, LLC. Prior to the Reorganization, all of Spero Therapeutics, LLC's directly held subsidiaries (including Spero Therapeutics, Inc.) were treated as corporations for U.S. federal income tax purposes and were subject to taxation in the United States or in other countries. Upon the Reorganization, Spero Therapeutics, Inc. became the parent company for Spero Therapeutics, LLC's former subsidiaries and these entities continue to be subject to taxation in the United States or in other countries. In each reporting period, the Company's tax provision includes the effects of consolidating the results of operations of its subsidiaries.

During the years ended December 31, 2019 and 2018, the Company recorded no income tax benefits for the net operating losses incurred in each year or interim period due to its uncertainty of realizing a benefit from those items.

The domestic and foreign components of loss before income taxes were as follows (in thousands):

	Year Ended December 31,	
	2019	2018
Domestic	$ (62,623)	$ (33,236)
Foreign	1,698	(8,426)
Loss before income taxes	$ (60,925)	$ (41,662)

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

	Year Ended December 31,	
	2019	2018
Federal statutory income tax rate	(21.0)	(21.0)
Federal and state research and development tax credit	(3.0)	(2.6)
State taxes, net of federal benefit	(6.7)	(5.4)
Foreign rate differential	(0.8)	1.9
Nondeductible items	1.1	1.2
Increase in deferred tax asset valuation allowance	30.4	25.9
Effective income tax rate	—	—

Net deferred tax assets as of December 31, 2019 and 2018 consisted of the following (in thousands):

	December 31,	
	2019	2018
Net operating loss carryforwards	$ 44,239	$ 29,025
Research and development tax credit carryforwards	5,220	3,385
Other	2,521	1,731
Total deferred tax assets	51,980	34,141
Valuation allowance	(51,980)	(34,141)
Net deferred tax assets	$ —	$ —

As of December 31, 2019, the Company had U.S. federal and state net operating loss carryforwards of $156.8 million and $157.8 million, respectively, which may be available to offset future income tax liabilities. The federal NOLs of $73.0 million will expire at various dates from 2033 to 2037 and approximately $83.8 million can be carried forward indefinitely. The state NOLs begin to expire in 2033 and will expire at various dates through 2039. In addition, as of December 31, 2019, the Company had foreign net operating loss carryforwards of $7.7 million, which may be available to offset future income tax liabilities and do not expire. As of December 31, 2019, the Company also had federal and state research and development tax credit carryforwards of $4.1 million and $1.1 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2033 and 2028, respectively.

Utilization of the U.S. net operating loss carryforwards 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, and corresponding provisions of state law, 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. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. Further, until a study is completed by the Company and any limitation is known, no amounts are being presented as an uncertain tax position.

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 deferred tax assets. Accordingly, a full valuation allowance has been established against the deferred tax assets as of December 31, 2019 and 2018. Management reevaluates the positive and negative evidence at each reporting period.

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2019 and 2018 related primarily to the increase in net operating loss carryforwards and research and development tax credit carryforwards, and were as follows (in thousands):

	December 31,	
	2019	2018
Valuation allowance as of beginning of year	$ (34,141)	$ (24,519)
Decreases recorded as benefit to income tax provision	—	—
Increases recorded to income tax provision	(17,839)	(9,622)
Valuation allowance as of end of year	$ (51,980)	$ (34,141)

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2019 or 2018. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision. As of December 31, 2019 or 2018, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts had been recognized in the Company's statement of operations and comprehensive loss.

The Company has not, as yet, conducted a study of its research and development credit carryforwards. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance.

Prior to the Reorganization, the Company filed separate U.S. income tax returns return for each of its subsidiaries. As a result of the Reorganization, the Company will file U.S. income tax returns as a U.S. consolidated group. In Massachusetts, the Company files income tax returns as a combined group except for its Massachusetts Securities Corporation subsidiary, which is a separate income tax filing. The statute of limitations for assessment by the Internal Revenue Service and Massachusetts tax authorities remains open for all years since 2015. 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 or state authorities to the extent utilized in a future period. No federal or state tax audits are currently in process.

On December 22, 2017, President Trump signed into law the "the Tax Cuts and Jobs Act" ("TCJA"). The TCJA includes a number of changes to existing tax law, including, among other things, a permanent reduction in the federal corporate income tax rate from a top marginal rate of 34% down to a flat rate of 21%, effective as of January 1, 2018, as well as limitation of the deduction for net operating losses to 80% of annual taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely).

As a result of the TCJA, the Company was required to revalue deferred tax assets and liabilities existing as of December 31, 2017 from the 34% federal rate in effect through the end of 2017, to the new 21%. This revaluation resulted in a reduction to the Company's deferred tax asset of $9.4 million. This amount was offset by a corresponding reduction in the valuation allowance. There was no impact to the Company's consolidated statements of operations and comprehensive loss as a result of the reduction in rates. The other provisions of the TCJA did not have a material impact on the Company's consolidated financial statements.

12. Commitments and Contingencies

License Agreements

The Company has entered into license agreements with various parties under which it is obligated to make contingent and non-contingent payments (see Note 14).

Operating Leases

The Company has entered into an operating lease agreement with U.S. REIF Central Plaza Massachusetts, LLC with respect to its corporate headquarters located at 675 Massachusetts Avenue, Cambridge, Massachusetts (see Note 5).

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company does not believe that the outcome of any claims under indemnification arrangements will have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2019 or 2018.

Legal Proceedings

The Company is not currently party to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses as incurred the costs related to such legal proceedings.

13. Government Contracts

BARDA

In July 2018, the Company was awarded a contract from BARDA of up to $44.2 million to develop tebipenem HBr for the treatment of complicated urinary tract infections (“cUTIs”) caused by antibiotic resistant Gram-negative bacteria and for assessment against biodefense pathogens. The award committed initial funding of $15.7 million over a three-year base period from July 1, 2018 to June 30, 2021 for cUTI development activities. In May 2019, the contract was modified to include additional funding of $2.5 million for SPR 994, increasing the amount of initial committed funding from $15.7 million to $18.1 million and increasing the overall potential award to $46.8 million. In January 2020, BARDA exercised its first contract option for additional committed funding of $15.9 million, increasing the total committed funding to $34.1 million. The balance of the award is subject to BARDA exercising a second option which would entail funding of $12.7 million and is exercisable by BARDA subject to, among other things, satisfactory progress and results from the biodefense studies described below.

As part of an inter-agency collaboration between BARDA and the Defense Threat Reduction Agency (“DTRA”), a series of studies to assess the efficacy of tebipenem HBr in the treatment of infections caused by biodefense threats such as anthrax, plague and melioidosis will be conducted by the U.S. Army Medical Research Institute of Infectious Diseases (“USAMRIID”) under the direction of Spero. Because the FDA requires data from a human pneumonic disease as supportive of use of an antibiotic to treat a biothreat infection, the scope of the BARDA award includes the assessment of tebipenem HBr levels in the lung of healthy volunteers as well as a proof of concept clinical trial in pneumonia patients. During the years ended December 31, 2019 and 2018, the Company recorded $12.1 million and $1.4 million of revenue under this agreement, respectively.

U.S. Department of Defense

On July 1, 2019, the Company received a $5.9 million award from the DoD Congressionally Directed Medical Research Programs (“CDMRP”) Joint Warfighter Medical Research Program. The funding will support the further clinical development of SPR206. The award commits non-dilutive funding of $5.9 million over a four-year period to cover the costs of select Phase 1 pharmacology studies, a 28-day GLP non-human primate toxicology study, and microbiological surveillance studies that would be required for a potential New Drug Application, or NDA, submission with the U.S. Food and Drug Administration for SPR206. During the year ended December 31, 2019, the Company recorded less than $0.1 million in revenue under this agreement.

In September 2016, the Company was awarded a cooperative agreement with the DoD to further develop anti-infective agents to combat Gram-negative bacteria. The agreement is structured as a single, two-year $1.5 million award. The Company is eligible for the full funding from the DoD, and there are no options to be exercised at a later date. The DoD funding supports next-generation potentiator discovery and screening of SPR741 partners. The Company recognizes revenue under this agreement as qualifying expenses are incurred. During the years ended December 31, 2019 and 2018, the Company recorded $0.2 million and $0.3 million in revenue under this agreement, respectively.

NIAID

In February 2017, the Company was awarded a grant from NIAID to conduct additional preclinical studies of SPR720, the Company's novel oral bacterial gyrase inhibitor, for the treatment of non-tuberculous mycobacterial infections. The award is structured as a 12-month $0.6 million base period and $0.4 million option period. In February 2018 NIAID exercised the $0.4 million 12-month option period. In January 2019, the period of performance for this award was extended for an additional 12-month period. During the years ended December 31, 2019 and 2018, the Company recorded $0.1 million and $0.5 million of revenue under this agreement, respectively.

In June 2016, the Company entered into agreements with Pro Bono Bio PLC ("PBB"), a corporation organized under the laws of England, and certain of its affiliates, including PBB Distributions Limited and Cantab Anti-Infectives Limited ("CAI"), in order to acquire certain intellectual property and government funding arrangements relating to SPR206. Under these agreements, CAI agreed to submit a request to NIAID to assign the then CAI-held NIAID contract to Spero, which was finalized in December 2017. The NIAID contract provides for development funding of up to $6.5 million over a base period and three option periods. As of December 31, 2018, funding for the base period and the first two option periods totaling $5.9 million have been committed. Spero shall pay PBB a percentage of funds received from NIAID up to a maximum of $1.3 million, of which $0.3 million was paid upfront to PBB as part of the agreement. During the years ended December 31, 2019 and 2018, the Company recorded $1.0 million and $1.4 million in revenue under this agreement, respectively.

CARB-X

In April 2017, the Company was awarded a grant from CARB-X, a public-private partnership funded by BARDA within the U.S. Department of Health and Human Services to be used to screen, identify and complete Phase 1 trials with at least one partner compound for SPR741. The award committed to funding of $1.5 million over a 12-month period. On March 12, 2018, CARB-X committed an additional $0.4 million related to the first option for a period from December 1, 2017 to March 31, 2018. There will be no additional options exercised under the CARB-X award. The Company recognized zero and $0.5 million of revenue in the years ended December 31, 2019 and 2018, respectively, under this agreement.

14. Collaboration and License Agreements

The Company has certain obligations under license agreements with third parties that include annual maintenance fees and payments that are contingent upon achieving various development, regulatory and commercial milestones. Pursuant to these license agreements, the Company is required to make milestone payments if certain development, regulatory and commercial milestones are achieved, and may have certain additional research funding obligations. Also, pursuant to the terms of each of these license agreements, when and if commercial sales of a product commence, the Company will pay royalties to its licensors on net sales of the respective products.

Vaxart (formerly Aviragen) Agreement

Under the Company's agreement with Vaxart for certain intellectual property and know-how relating to developing a gyrase inhibitor to develop therapies for Gram-negative infections, the Company was obligated to make milestone payments of up to an aggregate of $12.0 million upon the achievement of specified clinical, regulatory and commercial milestones and to pay royalties of low single-digit percentages based on net sales of products the Company acquired under the agreement. In November 2019, the Company and Vaxart entered into a stock repurchase agreement which terminated all of the Company's obligations to Vaxart.

Cantab License Agreement

Under the Cantab Agreements, the Company is obligated to make milestone payments of up to $5.8 million upon the achievement of specified clinical and regulatory milestones and a payment of £5.0 million ($6.6 million and $6.7 million as of December 31, 2019 and 2018, respectively)) upon the achievement of a specified commercial milestone. In addition, the Company has agreed to pay to PBB royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement. During the year ended December 31, 2018, the Company recorded $0.2 million in research and development expense related to the achievement of regulatory milestones for SPR206.

The Cantab Agreements continue indefinitely, with royalty payment obligations thereunder continuing on a product-by-product and country-by-country basis until the later of ten years after the first commercial sale of such product in such country or the expiration in such country of the last to expire valid claim of any of the applicable patents.

Vertex License Agreement

In May 2016, the Company entered into an agreement with Vertex Pharmaceuticals Incorporated ("Vertex") whereby Vertex granted the Company certain know-how and a sublicense to research, develop, manufacture and sell products for a proprietary compound, as well as a transfer of materials. In exchange for the know-how, sublicense and materials, Spero paid Vertex an upfront, one-time, nonrefundable, non-creditable fee of $0.5 million, which was recognized as research and development expense. As part of the agreement, the Company is obligated to make future milestone payments of up to $81.1 million upon the achievement of specified clinical, regulatory and commercial milestones and to pay Vertex tiered royalties, on a product-by-product and country-by-country basis, of a mid single-digit to low double-digit percentage based on net sales of products licensed under the agreement. During the year ended December 31, 2018, the Company recorded $0.2 million in research and development expense related to the achievement of regulatory milestones for SPR720.

The agreement continues in effect until the expiration of all payment obligations thereunder, with royalty payment obligations continuing on a product-by-product and country-by-country basis until the later of ten years after the first commercial sale of such product in such country or the date of expiration in such country of the last to expire applicable patent. Further, Vertex has the right to terminate the agreement if provided with notification from the Company of intent to cease all development or if no material development or commercialization efforts occur for one year.

Meiji License Agreement

In June 2017, the Company entered into agreements with Meiji Seika Pharma Co. Ltd. ("Meiji"), a Japanese corporation, whereby Meiji granted to the Company certain know-how and a license to research, develop, manufacture and sell products for a proprietary compound in the licensed territory. In exchange for the know-how and license, the Company paid Meiji an upfront, one-time, nonrefundable, non-creditable fee of $0.6 million, which was recognized as research and development expense. As part of the agreement, the Company is obligated to make milestone payments of up to $3.0 million upon the achievement of specified clinical and regulatory milestones, to pay royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement and to pay Meiji a low double-digit percentage of any sublicense fees received by the Company up to $7.5 million. In October 2017, the Company paid a $1.0 million milestone payment to Meiji upon the enrollment of the first patient in the Company's Phase 1 clinical trial of tebipenem HBr. The payment was recorded as research and development expense in the statement of operations and comprehensive loss for the year ended December 31, 2017. During the three months ended December 31, 2018, the Company paid Meiji $1.6 million related to fixed assets which will be used in manufacturing related activities at Meiji. This equipment has been capitalized as property and equipment in the consolidated balance sheet as of December 31, 2018.

The agreement continues in effect until the expiration of all payment obligations thereunder (including royalty payments and licensee revenue) on a product-by-product and country-by-country basis, unless earlier terminated by the parties. Pursuant to the terms of the agreement, in addition to each party's right to terminate the agreement upon the other party's material breach (if not cured within a specified period after receipt of notice) or insolvency, the Company also has unilateral termination rights (i) in the event that the Company abandons the development and commercialization of tebipenem HBr for efficacy, safety, legal or business factors, and (ii) under certain circumstances arising out of the head license with a global pharmaceutical company.

Northern License Agreement

In June 2017, in connection with the repurchase of all of the outstanding shares of Spero Potentiator, the Company amended its license agreement with Northern such that the Company agreed to pay Northern up to $7.0 million upon the achievement of specified clinical, regulatory and other milestones, including a total payment of $2.5 million upon the closing of an initial public offering. In addition, under an exchange agreement the Company entered into with Northern, the Company is obligated to make a payment to Northern of $0.1 million upon the closing of an initial public offering. The agreement had a perpetual term and no express termination rights. Upon the closing of the Company's IPO in November 2017, the Company paid $2.6 million to Northern in connection with both the license and exchange agreements. This payment was recorded as research and development expense in the Company's statement of operations and comprehensive loss for the year ended December 31, 2017. The Company and Northern terminated the agreement effective January 1, 2020.

Everest Medicines License Agreement

On January 4, 2019, the Company, through its wholly owned subsidiary New Pharma License Holdings Limited ("NPLH"), entered into a license agreement (the "Everest License Agreement"), with Everest Medicines II Limited. Under the terms of the Everest License Agreement, the Company granted Everest an exclusive license to develop, manufacture and commercialize SPR206 or products that contain SPR206 (the "Licensed Products"), in Greater China (which includes Mainland China, Hong Kong and Macau), South Korea and certain Southeast Asian countries (the "Territory"). The Company retained development, manufacturing and commercialization rights with respect to SPR206 and Licensed Products in the rest of the world and also retained the right to develop or manufacture SPR206 and Licensed Products in the Territory for use outside the Territory. In addition to the license grant with respect to SPR206, the Company, through its wholly owned subsidiary, Spero Potentiator, Inc., a Delaware corporation, granted Everest a 12-month exclusive option to negotiate with it for an exclusive license to develop, manufacture and commercialize SPR741 in the Territory.

Under the terms of the Everest License Agreement, the Company received an upfront payment of $3.0 million, comprised of a $2.0 million payment to license SPR206 and $1.0 million for the exclusive option to negotiate a license to develop SPR741. The Company will receive a milestone payment of $2.0 million upon completion and delivery of the results of a clinical study and future milestones of up to $1.5 million if the Company chooses to complete a future clinical study. The Company may also receive up to an additional $55.0 million in milestone payments upon Everest's achievement of certain developmental, regulatory and sales milestone events related to SPR206, which achievement cannot be guaranteed. The Company is also entitled to receive high single-digit to low double-digit royalties on net sales, if any, of Licensed Products in the Territory following regulatory approval of SPR206. Everest has the right to sublicense to affiliates and third parties in the Territory.

Everest is responsible for all costs related to developing, obtaining regulatory approval of and commercializing SPR206 and Licensed Products in the Territory, and is obligated to use commercially reasonable efforts to develop, manufacture and commercialize Licensed Products, including to achieve certain specified diligence milestones within agreed-upon periods. A joint development committee will be established between the Company and Everest to coordinate and review the development, manufacturing and commercialization plans with respect to Licensed Products in the Territory.

Unless earlier terminated due to certain material breaches of the contract, or otherwise, the Everest License Agreement will expire on a jurisdiction-by-jurisdiction and Licensed Product-by-Licensed Product basis until the latest to occur of expiration of the last valid claim under a licensed patent in such jurisdiction, the expiration of regulatory exclusivity in such jurisdiction or ten years after the first commercial sale of such Licensed Product in such jurisdiction. The Everest License Agreement may be terminated in its entirety by Everest upon 90 or 180 days' prior written notice, depending on the stage of development of the initial Licensed Product.

Accounting Analysis and Revenue Recognition

The Company determined the Everest License Agreement to be under the scope of ASC 606. Accordingly, in determining the appropriate amount of revenue to be recognized, the Company performed the following steps: (i) identified the promised goods or services in the contract; (ii) determined whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measured the transaction price, including the constraint on variable consideration; (iv) allocated the transaction price to the identified performance obligations in proportion to their SSP; and (v) recognized revenue when each performance obligation was deemed to be satisfied.

Based on that evaluation, the Company identified three performance obligations, as presented below. The transaction price to be allocated to the identified performance obligations was determined to be $5.0 million consisting of: (i) the license upfront fee of $2.0 million, (ii) the $1.0 million exclusive option to negotiate a license to develop SPR741, and (iii) research and development services related to an upcoming milestone of $2.0 million that is deemed to be probable to be achieved. The additional clinical study that is at the Company's discretion to perform is considered a marketing offering and therefore not included in the assessment at contract inception. The Company determined that the license was distinct from the exclusive option for SPR 741 and the research and development services. The following table shows the performance obligations, along with their SSP and the transaction price allocated to those obligations (in thousands):

Performance Obligations	Standalone Selling Price	Transaction Price Allocated	Recognition Method
License and know-how transfer (1)	$ 9,858	$ 3,553	Fully satisfied; recognized upon delivery of the license
Exclusive option on SPR741	400	144	Recognized in Q4 2019 upon the return of the IP rights to Northern
Research and development services (2)	3,614	1,303	Recognized over time as services are delivered through the expected completion date of Q2 2020
		$ 5,000	

(1) The standalone selling price for the license and know-how transfer was determined using the residual approach, corroborated by internal cost estimates.

(2) The standalone selling price for the research and development services was estimated using management's best estimate of the cost of obtaining these services at arm's length from a third-party provider and using internal full time equivalent costs to support the development services.

During the year ended December 31, 2019, the Company recognized $4.7 million of revenue related to this agreement. As of December 31, 2019, the aggregate amount of the transaction price allocated to performance obligations that are partially unsatisfied was $0.3 million. The Company has a contract asset of $1.7 million, which is included in prepaid expenses and other current assets in the condensed consolidated balance sheet as of December 31, 2019.

Gates MRI

In June 2019, the Company entered into a collaboration with Gates MRI to develop SPR720 for the treatment of lung infections caused by Mycobacterium tuberculosis ("Mtb"). In furtherance of the Gates MRI's charitable purposes, the Company also granted to Gates MRI a no-cost, exclusive license to develop, manufacture and commercialize SPR720 for the treatment of tuberculosis ("TB") in low- and middle- income countries. The Gates MRI is responsible for formulating and funding its own research plan for the development of SPR720 for TB. As such, Gates MRI will conduct and fund preclinical and clinical studies for the development of SPR720 against TB. In addition, Gates MRI and the Company will jointly design and manage certain collaborative research activities, which the Company will perform and which will be funded by the Gates MRI. Due to the cost-funded nature of the payments and the Company's assessment that it does not have a vendor/customer relationship with the Gates MRI, the Company will recognize the funding received under the agreement as a reduction to the research and development expenses incurred, as the related expenses are incurred. During the twelve months ended December 31, 2019, the Company recorded $1.7 million as a reduction to research and development expense related to activities funded by Gates MRI.

15. Australia Research and Development Tax Incentive

The Australian government has established a research and development tax incentive to encourage industry investment in research and development, which is available to companies incorporated under Australian law that have core research and development activities. In September 2016, the Company established Spero Potentiator Australia Pty Limited to carry out certain research and development activities. As this subsidiary meets the eligibility requirements of the Australian tax law, it is eligible to receive a 43.5% tax incentive for qualified research and development activities. For the years ended December 31, 2019 and 2018, $0.4 million and $1.2 million, respectively, was recorded as a reduction to research and development expenses in the consolidated statements of operations and comprehensive loss associated with this tax incentive, representing 43.5% of the Company's qualified research and development spending in Australia. The refund is denominated in Australian dollars and, therefore, the receivable is re-measured to U.S. dollars as of each reporting date. As of December 31, 2019 and 2018, the Company's tax incentive receivables from the Australian government totaled $0.8 million and $1.1 million, respectively.

16. Net Loss per Share

Basic and diluted net loss per share attributable to common stockholders of Spero Therapeutics, Inc. was calculated as follows (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2019	2018
Numerator:		
Net loss	$ (60,925)	$ (41,662)
Denominator:		
Weighted average common shares outstanding, basic and diluted	18,160,525	16,001,832
Net loss per share, basic and diluted	$ (3.35)	$ (2.60)

Per Note 19 to the Financial Statements, the Company announced a rights offering in February 2020 that settled on March 5, 2020. The rights offering contained a bonus element, whereby the exercise price at issuance was less than the fair value of the stock on the date of settlement. When a bonus element exists, the Company is required to reflect the impact of the bonus element retroactively on basic and diluted EPS for the periods ending December 31, 2019 and 2018. It was determined that the bonus element related to the rights offering in 2020 had no impact on basic or diluted EPS for the periods ending December 31, 2019 and 2018.

The Company excluded potentially dilutive securities from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders of Spero Therapeutics, Inc. is the same. The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2019	2018
Options to purchase common stock	2,969,428	2,297,810
Unvested restricted stock units	40,750	—
Series A convertible preferred stock (as converted to common shares)	1,720,000	2,220,000
Series B convertible preferred stock (as converted to common shares)	1,000,000	1,000,000
Total	5,730,178	5,517,810

17. Retirement Plan

The Company has a defined-contribution plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pre-tax basis. As currently established, the Company is not required to make any contributions to the 401(k) Plan. In 2019, the Company began to make matching contributions to the 401(k) Plan. The Company did not make any matching contributions during the years ended December 31, 2018.

18. Quarterly Financial Data (unaudited)

	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
Grant revenue	$ 3,911	$ 2,089	$ 4,471	$ 2,934
Collaboration revenue	3,807	67	172	696
Operating expenses	13,414	15,808	22,628	29,513
Net loss	(5,072)	(13,150)	(17,717)	(24,986)
Net loss per share attributable to common shareholders per share, basic and diluted	$ (0.29)	$ (0.74)	$ (0.95)	$ (1.31)
Weighted average shares outstanding, basic and diluted:	17,221,120	17,667,620	18,659,079	19,052,827

	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
Grant revenue	$ 1,153	$ 463	$ 658	$ 1,692
Operating expenses	11,969	10,434	11,593	12,776
Net loss	(10,644)	(9,956)	(10,463)	(10,599)
Net loss per share attributable to common shareholders per share, basic and diluted	$ (0.74)	$ (0.69)	$ (0.60)	$ (0.60)
Weighted average shares outstanding, basic and diluted:	14,369,182	14,376,529	17,471,462	17,736,996

19. Subsequent Events

On February 11, 2020, the Company announced a rights offering pursuant to which it distributed to holders of its common stock and Series A Preferred Stock and Series B Preferred Stock, at no charge, non-transferable subscription rights to purchase shares of Spero common stock and Series C Convertible Preferred Stock ("Series C Preferred Stock"), with an aggregate offering value of $30.0 million. For each share of common stock (including shares of common stock issuable upon conversion of the Company's outstanding shares of Series A Preferred Stock and Series B Preferred Stock) owned by holders of record as of 5:00 p.m., New York time, on February 10, 2020, such holders received 0.152 rights to purchase shares of Spero common stock (subject to the aggregate offering threshold and certain ownership limitations). Each whole right allowed holders to subscribe for one share of common stock at the subscription price equal to $9.00 per whole share (or an equivalent number of shares of Series C Preferred Stock). The total number of subscription rights issued to each stockholder was rounded down to the nearest whole number.

Any participant in the rights offering that, following exercise of such participant's subscription right, would be or become a holder of greater than 9.99% of the outstanding number of shares of the Company's common stock following the offering may elect to instead purchase Series C Preferred Stock at a purchase price of $9,000 per share (ratably adjusted for fractional shares), and any such holder so electing would have a right to purchase one one-thousandth of a share of Series C Preferred Stock for each share of common stock it had a right to purchase under the subscription rights. Each share of Series C Preferred Stock is convertible into 1,000 shares of Spero common stock at the election of the holder, subject to beneficial ownership conversion limits applicable to the Series C Preferred Stock. The Series C Preferred Stock generally have no voting rights, except as required by law, and participate pari passu (on an as-converted basis) with any distribution of proceeds to holders of common stock and Series A Preferred Stock and Series B Preferred Stock, in the event of the Company's liquidation, dissolution or winding up or the payment of a dividend on the common stock.

At the closing of the rights offering on March 5, 2020, a total of 1,046,249 shares of the Company's common stock and 2,287 shares of Series C Preferred Stock were issued for aggregate gross proceeds of $30.0 million.

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2019. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2019, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Controls Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with general accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the 2013 framework in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under that framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2019.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for "emerging growth companies".

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended December 31, 2019 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Directors

Set forth below are the names of our directors, their ages, their offices in the Company, if any, their principal occupations or employment for at least the past five years, the length of their tenure as directors and the names of other public companies in which such persons hold or have held directorships during the past five years. Additionally, information about the specific experience, qualifications, attributes or skills that led to our Board of Directors' conclusion that each person listed below should serve as a director is set forth below:

Name	Age	Position with the Company
Milind Deshpande, Ph.D.	63	Chairman of the Board of Directors
Jean-François Formela, M.D.	63	Director
Ankit Mahadevia, M.D.	39	Chief Executive Officer, President and Director
John C. Pottage, Jr., M.D.	67	Director
Cynthia Smith	51	Director
Frank E. Thomas	50	Director
Patrick Vink, M.D.	56	Director

Our Board of Directors has reviewed the materiality of any relationship that each of our directors has with Spero Therapeutics, Inc., either directly or indirectly. Based upon this review, our Board of Directors has determined that the following members of the Board of Directors are "independent directors" as defined by The Nasdaq Stock Market: Milind Deshpande, Ph.D., Jean-François Formela, M.D., John C. Pottage, Jr., M.D., Cynthia Smith, Frank E. Thomas, and Patrick Vink, M.D. See "Item 13. Certain Relationships and Related Transactions, and Director Independence."

Milind Deshpande, Ph.D. has served on our Board of Directors since January 2014 and currently serves as chairman of our Board of Directors. Dr. Deshpande is the President and Chief Executive Officer at Nayan Therapeutics since February 2019, and President & CEO of Avilar Therapeutics since January 2020. He is also a Venture Partner at RA Capital, where he has served since October 2018. Dr. Deshpande joined Achillion Pharmaceuticals, Inc. in September 2001 as Vice President of Chemistry, was named Head of Drug Discovery in April 2002, Senior Vice President of Drug Discovery in December 2002, Senior Vice President and Chief Scientific Officer in December 2004 and Executive Vice President of Research and Chief Scientific Officer in June 2007. He was promoted to President of Research and Development in October 2010. In May 2013, Dr. Deshpande was appointed President and Chief Executive Officer of Achillion and joined its board of directors on which he served until May 2018. Prior to joining Achillion, Dr. Deshpande was Associate Director of Lead Discovery and Early Discovery Chemistry at the Pharmaceutical Research Institute at Bristol-Myers Squibb Co. from 1991 to 2001, where he managed the identification of new clinical candidates to treat infectious and neurological diseases. From 1988 to 1991, he held a faculty position at Boston University Medical School. Dr. Deshpande received his Ph.D. in Organic Chemistry from Ohio University, following his undergraduate education in India. We believe that Dr. Deshpande is qualified to serve on our Board of Directors due to his extensive experience in the life sciences industry.

Jean-François Formela, M.D. has served on our Board of Directors since March 2013. Dr. Formela is currently a partner at Atlas Venture and focuses on novel drug discovery approaches and therapeutics. He joined Atlas Venture in 1993 to build the U.S. life sciences franchise. He is a director and co-founder of IFM Therapeutics, Intellia Therapeutics (Nasdaq: NTLA), Korro Bio, Triplet Therapeutics and Translate Bio (Nasdaq: TBIO). Jean-François also serves on the boards of F-star and Ikena Oncology. His prior investments include Adnexus, ArQule (Nasdaq: ARQL), Arteaus Therapeutics (acquired by Eli Lilly), CoStim Pharmaceuticals (acquired by Novartis), deCODE (Nasdaq: DCGN), Exelixis (Nasdaq: EXEL) and NxStage (Nasdaq: NXTM). Dr. Formela is a member of the Partners Healthcare Innovation Advisory Board and a former trustee of the Boston Institute of Contemporary Art. He received his M.D. from Paris University School of Medicine and his M.B.A. from Columbia University. We believe Dr. Formela's experience in the life sciences industry, as well as his practice of medicine, provides him with the qualifications and skills to serve as a director of our Company.

Ankit Mahadevia, M.D. has served as our Chief Executive Officer and President since March 2015 and has been a member of our Board of Directors since September 2013. He was formerly a Venture Partner in the life sciences group at Atlas Venture, located in Cambridge, Massachusetts. In that capacity he supported the formation of eight companies focused on novel drug discovery platforms and therapeutic products, including Nimbus Therapeutics, Arteaus Therapeutics (acquired by Lilly), and Translate Bio (Nasdaq: TBIO). He led three of these companies as acting CEO, including Synlogic (Nasdaq: SYBX). Prior to joining Atlas Venture in 2008, Dr. Mahadevia worked on product and business development with the founding team at Arcion Therapeutics, Inc. He has also held positions in business development both at Genentech, Inc. and at Vanda Pharmaceuticals Inc. Previously, he worked in the health care groups of McKinsey & Company and Monitor Group. Dr. Mahadevia began his career in health care policy, with roles in the U.S. Senate Health, Education, Labor, and Pensions committees, the U.S. Government Accountability Office and the Mexican Institute of Social Security. He has spoken widely on entrepreneurship, including at Harvard Univesity, Columbia University, Northwestern University, and the Berkeley Forum. Dr. Mahadevia has also been active in the policy of life science innovation, including service on the Advisory Council at the NIH National Center for Advancing Translational Sciences. Dr. Mahadevia holds an M.D. from the Johns Hopkins School of Medicine, an M.B.A. from the Wharton School at the University of Pennsylvania and a B.A. in Economics and Biology from Northwestern University. We believe that Dr. Mahadevia is qualified to serve on our Board of Directors due to his experience serving as our Chief Executive Officer and President and his extensive experience in the life sciences industry.

John C. Pottage, Jr., M.D. has served on our Board of Directors since September 2018. Dr. Pottage served as Senior Vice President and Chief Scientific and Medical Officer of ViiV Healthcare from November 2009 to October 2019. From September 2008 to November 2009, Dr. Pottage served as Senior Vice President, Head of Infectious Disease Medicine Development Center and, from June 2007 to September 2008, as the Vice President, Global Clinical Development of Antivirals, at GlaxoSmithKline. Prior to joining GlaxoSmithKline, Dr. Pottage served as Chief Medical Officer and Senior Vice President of Drug Development of Achillion Pharmaceuticals from May 2002 to May 2007. From July 1998 to May 2002, Dr. Pottage served as Medical Director of Vertex Pharmaceuticals. We believe that Dr. Pottage's extensive industry and executive experience, his broad experience within the biopharmaceutical sector and his knowledge of the life sciences industry qualifies him to serve on our Board of Directors.

Cynthia Smith has served on our Board of Directors since March 2019. Ms. Smith was Chief Commercial Officer of ZS Pharma, from June 2013 to December 2016. ZS Pharma became a subsidiary of AstraZeneca after its acquisition in December 2015. Prior to joining ZS Pharma, Ms. Smith was Vice President, Market Access & Commercial Development at Affymax, Inc., a biotechnology company focused on the development and commercialization of novel renal therapies, including a new anemia drug for chronic kidney disease patients. Ms. Smith was employed at Affymax from October 2008 to March 2013. Prior to Affymax, Ms. Smith was Executive Director of Healthcare System and Medicare Strategy at Merck. During her tenure at Merck from June 2000 to October 2008, she also held various leadership positions in corporate strategy, public policy, and external affairs, including global crisis management for the Vioxx recall. Before joining the pharmaceutical industry, she served in the White House Office of Management and Budget (OMB) in the Clinton Administration. Ms. Smith earned an MBA from the Wharton School of the University of Pennsylvania, an MS in public policy from the Eagleton Institute of Politics at Rutgers University, and a BA from the University of North Carolina at Chapel Hill. Ms. Smith also serves on the boards of directors of Dicerna Pharmaceuticals and Akebia Therapeutics. We believe that Ms. Smith's extensive management experience in the healthcare industry and her experience as a member of the board of directors of other publicly traded biotechnology companies, as well as her broad life sciences industry knowledge, qualifies her to serve on our Board of Directors.

Frank E. Thomas has served on our Board of Directors since July 2017. Mr. Thomas is currently Chief Operating Officer and Chief Financial Officer of Orchard Therapeutics, a development-stage biotechnology company based in the United Kingdom, where he served as Chief Financial Officer and Chief Business Officer from January 2018 to December 2019. Prior to Orchard, Mr. Thomas served as the President and Chief Operating Officer of AMAG Pharmaceuticals, Inc., a publicly traded commercial-stage pharmaceutical company, from April 2015 to April 2017, as AMAG's Executive Vice President and Chief Operating Officer from May 2012 through April 2015 and as Executive Vice President, Chief Financial Officer and Treasurer from August 2011 through May 2012. Prior to AMAG, he served as Senior Vice President, Chief Operating Officer and Chief Financial Officer for Molecular Biometrics, Inc., a commercial-stage medical diagnostics company, from October 2008 to July 2011. Prior to Molecular Biometrics, Mr. Thomas spent four years at Critical Therapeutics, Inc., a public biopharmaceutical company, from April 2004 to March 2008, where he was promoted to President in June 2006 and Chief Executive Officer in December 2006 from the position of Senior Vice President and Chief Financial Officer. He also served on the board of directors of Critical Therapeutics from 2006 to 2008. Prior to 2004, Mr. Thomas served as the Chief Financial Officer and Vice President of Finance and Investor Relations at Esperion Therapeutics, Inc., a public biopharmaceutical company. Mr. Thomas was a member of the board of directors of the Massachusetts Biotechnology Council from 2007 to 2015 and currently serves as a member of the board of directors of Zafgen, Inc., a public biopharmaceutical company, which he joined in June 2014. Mr. Thomas holds a B.B.A. from the University of Michigan, Ann Arbor. We believe that Mr. Thomas' extensive commercial and operational management experience at biopharmaceutical companies and with financial matters qualifies him to serve on our Board of Directors.

Patrick Vink, M.D. has served on our Board of Directors since September 2015. Dr. Vink has been an advisor to the pharmaceutical industry since 2015 and non-executive board member of several companies. Previously, Dr. Vink was employed at Cubist Pharmaceuticals, Inc. Most recently, he served as Executive Vice-President and Chief Operating Officer, overseeing all worldwide commercial and technical operations as well as global alliance management and managing the company's profit and loss. He joined Cubist in 2012 as Senior Vice-president and Head of all International Business Operations. In this role, he was responsible for the all business activities in International markets outside USA. Prior to joining Cubist, Dr. Vink served as Senior Vice President, Global Head of Hospital Business and Global Head of Biologics for Mylan Inc. In this role, Dr. Vink managed the global hospital business of the company. He joined Mylan in 2008 and established a number of global functions for the company in Switzerland. Before joining Mylan, Dr. Vink held several leadership positions across the industry, including Head of Global Business Franchise Biopharmaceuticals for Novartis Sandoz; Vice-President International Business for Biogen, Inc.; and Head of Worldwide Marketing, Cardiovascular and Thrombosis for Sanofi-Synthélabo SA. Dr. Vink served as a member of the Executive Committee of the European Federation of Pharmaceutical Industries and Associations (EFPIA) between 2013 and 2015. Dr. Vink graduated as a medical doctor from the University of Leiden, Netherlands in 1988 and obtained his M.B.A. in 1992 from the University of Rochester. Dr. Vink serves on the boards of directors of Santhera Pharmaceuticals AG, Amryt Pharma PLC., and is Chairman of the board of directors of Targovax Oy, Acacia Pharma and two privately held companies. We believe that Dr. Vink is qualified to serve on our Board of Directors because of his extensive operational business experience, significant knowledge of the activities of our company, and diverse background serving on the board of directors of various public and private life science companies.

Term of Office of Directors

Our amended and restated By-Laws provide that our business is to be managed by or under the direction of our Board of Directors. Our Board of Directors is divided into three classes for purposes of election. One class is elected at each annual meeting of stockholders to serve for a three-year term. Our Board of Directors currently consists of seven members, classified into three classes as follows:

(1) Milind Deshpande, Ph.D., Jean-François Formela, M.D. and Ankit Mahadevia, M.D. constitute our Class III directors with a term ending at the 2020 annual meeting;

(2) Cynthia Smith and John C. Pottage, Jr., M.D. constitute our Class I directors with a term ending at the 2021 annual meeting; and

(3) Patrick Vink, M.D. and Frank E. Thomas constitute our Class II directors with a term ending at the 2022 annual meeting.

Committees of the Board of Directors and Meetings

Meeting Attendance. During the fiscal year ended December 31, 2019, there were four meetings of our Board of Directors, and the various committees of the Board of Directors met a total of nine times. No director attended fewer than 75% of the total number of meetings of the Board of Directors and of committees of the Board of Directors on which he served during fiscal 2019. The Board of Directors has adopted a policy under which each member of the Board of Directors makes every effort to but is not required to attend each annual meeting of our stockholders.

Audit Committee. Our Audit Committee met four times during fiscal 2019. This committee currently has three members, Frank E. Thomas (Chairman), John C. Pottage, Jr., M.D., and Patrick Vink, M.D. Our Audit Committee's role and responsibilities are set forth in the Audit Committee's written charter and include the authority to retain and terminate the services of our independent registered public accounting firm. In addition, the Audit Committee reviews annual financial statements, considers matters relating to accounting policy and internal controls and reviews the scope of annual audits. All members of the Audit Committee satisfy the current independence standards promulgated by the Securities and Exchange Commission and by The Nasdaq Stock Market, as such standards apply specifically to members of audit committees. The Board of Directors has determined that Mr. Thomas is an "audit committee financial expert," as the Securities and Exchange Commission has defined that term in Item 407 of Regulation S-K. Please also see the report of the Audit Committee set forth elsewhere in this proxy statement.

A copy of the Audit Committee's written charter is publicly available on our website at www.sperotherapeutics.com.

Compensation Committee. Our Compensation Committee met four times during fiscal 2019. This committee currently has four members, Patrick Vink, M.D. (Chairman), Jean-François Formela, M.D., Milind Deshpande, Ph.D., and Cynthia Smith. Our Compensation Committee's role and responsibilities are set forth in the Compensation Committee's written charter and includes reviewing, approving and making recommendations regarding our compensation policies, practices and procedures to ensure that legal and fiduciary responsibilities of the Board of Directors are carried out and that such policies, practices and procedures contribute to our success. Our Compensation Committee also administers the Spero Therapeutics, Inc. 2017 Stock Incentive Plan, as amended, or the 2017 Plan. The Compensation Committee is responsible for the determination of the compensation of our chief executive officer, and shall conduct its decision making process with respect to that issue without the chief executive officer present. All members of the Compensation Committee qualify as independent under the definition promulgated by The Nasdaq Stock Market.

The Compensation Committee engaged Pearl Meyer & Partners, LLC ("Pearl Meyer") as an independent advisor to the Compensation Committee providing executive compensation consulting services. Pearl Meyer was engaged by and reports solely to the Compensation Committee. The Compensation Committee has the sole authority to approve the terms of the engagement. Pearl Meyer did not provide any services to the Company other than executive compensation consulting services during fiscal year 2019. In compliance with the SEC and the corporate governance rules of The Nasdaq Stock Market, Pearl Meyer provided the Compensation Committee with a letter addressing each of the six independence factors. Their responses affirm the independence of Pearl Meyer and the partners, consultants, and employees who service the Compensation Committee on executive compensation matters and governance issues.

A copy of the Compensation Committee's written charter is publicly available on our website at www.sperotherapeutics.com.

Nominating and Corporate Governance Committee. Our Nominating and Corporate Governance Committee ("Nominating Committee") met once during fiscal 2019 and has three members, Milind Deshpande, Ph.D. (Chairman), Jean-François Formela, M.D., and Frank E. Thomas. Our Board of Directors has determined that all members of the Nominating Committee qualify as independent under the definition promulgated by The Nasdaq Stock Market. The Nominating Committee's responsibilities are set forth in the Nominating Committee's written charter and include:

- identifying and recommending candidates for membership on our Board of Directors;
- recommending directors to serve on board committees;
- reviewing and recommending our corporate governance guidelines and policies;
- reviewing proposed waivers of the code of conduct for directors and executive officers;
- evaluating, and overseeing the process of evaluating, the performance of our Board of Directors and individual directors; and
- assisting our Board of Directors on corporate governance matters.

Generally, our Nominating Committee considers candidates recommended by stockholders as well as from other sources such as other directors or officers, third party search firms or other appropriate sources. Once identified, the Nominating Committee will evaluate a candidate's qualifications in accordance with the criteria set forth in our Corporate Governance Guidelines. Our Nominating Committee has not adopted a formal diversity policy in connection with the consideration of director nominations or the selection of nominees. However, the Nominating Committee will consider issues of diversity among its members in identifying and considering nominees for director, and strive where appropriate to achieve a diverse balance of backgrounds, perspectives, experience, age, gender, ethnicity and country of citizenship on the Board of Directors and its committees.

If a stockholder wishes to propose a candidate for consideration as a nominee for election to the Board of Directors, it must follow the procedures described in our amended and restated By-Laws and in "Stockholder Proposals and Nominations For Director" at the end of this proxy statement. Any such recommendation should be made in writing to the Nominating and Governance Committee, care of our Secretary at our principal office and should be accompanied by the following information concerning each recommending stockholder and the beneficial owner**,** if any, on whose behalf the nomination is made:

- all information relating to such person that would be required to be disclosed in a proxy statement;
- certain biographical and share ownership information about the stockholder and any other proponent, including a description of any derivative transactions in the Company's securities;
- a description of certain arrangements and understandings between the proposing stockholder and any beneficial owner and any other person in connection with such stockholder nomination; and
- a statement whether or not either such stockholder or beneficial owner intends to deliver a proxy statement and form of proxy to holders of voting shares sufficient to carry the proposal.

The recommendation must also be accompanied by the following information concerning the proposed nominee:

- certain biographical information concerning the proposed nominee;
- all information concerning the proposed nominee required to be disclosed in solicitations of proxies for election of directors;
- certain information about any other security holder of the Company who supports the proposed nominee;

- a description of all relationships between the proposed nominee and the recommending stockholder or any beneficial owner, including any agreements or understandings regarding the nomination; and
- additional disclosures relating to stockholder nominees for directors, including completed questionnaires and disclosures required by our amended and restated By-Laws.

Corporate Governance Guidelines. Our Board of Directors has adopted corporate governance guidelines, which apply to our principal executive officer, our principal financial and accounting officer and all of our other employees, to assist in the exercise of its duties and responsibilities and to serve the best interests of our Company and our stockholders. The guidelines provide that:

- our Board of Directors' principal responsibility is to oversee the management of our Company;
- except as required by Nasdaq rules, a majority of the members of our Board of Directors must be independent directors;
- the independent directors meet in executive session at least twice a year;
- directors have full and free access to management and, as necessary, independent advisors; and
- our nominating and corporate governance committee will oversee periodic self-evaluations of the Board of Directors to determine whether it and its committees are functioning effectively.

We have no formal policy regarding diversity of our board members, but our Corporate Governance Guidelines provide that the background and qualifications of the members of our Board of Directors considered as a group should provide a significant breadth of experience, knowledge, and ability to assist our Board of Directors in fulfilling its responsibilities. Our priority in selection of board members is identification of members who will further the interests of our stockholders through their established records of professional accomplishment, the ability to contribute positively to the collaborative culture among our board members, knowledge of our business, understanding of the competitive landscape in which we operate and adherence to high ethical standards.

Copies of the Nominating Committee's written charter and our Corporate Governance Guidelines are publicly available on the Company's website at www.sperotherapeutics.com.

Code of Conduct and Ethics. We have adopted a Code of Business Conduct and Ethics that applies to all of our employees, including our chief executive officer and chief financial and accounting officers. The text of the Code of Business Conduct and Ethics is posted on our website at www.sperotherapeutics.com and will be made available to stockholders without charge, upon request, in writing to the Secretary of the Company at Spero Therapeutics, Inc., 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts 02139. Disclosure regarding any amendments to, or waivers from, provisions of the Code of Business Conduct and Ethics that apply to our directors, principal executive and financial officers will be included in a Current Report on Form 8-K within four business days following the date of the amendment or waiver, unless website posting or the issuance of a press release of such amendments or waivers is then permitted by the rules of The Nasdaq Stock Market.

Compensation Committee Interlocks and Insider Participation. None of the members of our Compensation Committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of our Board of Directors or Compensation Committee of any entity that has one or more executive officers serving on our Board of Directors or Compensation Committee. For a description of transactions between us and members of our Compensation Committee and affiliates of such members, see "Certain Relationships and Related Person Transactions."

Board Leadership Structure and Role in Risk Oversight

The Company's Board of Directors is currently chaired by Milind Deshpande, Ph.D.. As a general policy, our Board of Directors believes that separation of the positions of chairman and chief executive officer reinforces the independence of our Board of Directors from management, creates an environment that encourages objective oversight of management's performance and enhances the effectiveness of our Board of Directors as a whole. As such, Dr. Mahadevia serves as our Chief Executive Officer while Dr. Deshpande serves as the chairman of our Board of Directors but is not an officer.

Our Board of Directors oversees the management of risks inherent in the operation of our business and the implementation of our business strategies. Our Board of Directors performs this oversight role by using several different levels of review. In connection with its reviews of the operations and corporate functions of our Company, our Board of Directors addresses the primary risks associated with those operations and corporate functions. In addition, our Board of Directors reviews the risks associated with the Company's business strategies periodically throughout the year as part of its consideration of undertaking any such business strategies.

Each of our board committees also oversees the management of the Company's risk that falls within the committee's areas of responsibility. In performing this function, each committee has full access to management, as well as the ability to engage advisors. Our Chief Executive Officer reports to the Audit Committee and is responsible for identifying, evaluating and implementing risk management controls and methodologies to address any identified risks. In connection with its risk management role, our Audit Committee meets privately with representatives from our independent registered public accounting firm and our Chief Executive Officer. The Audit Committee oversees the operation of our risk management program, including the identification of the primary risks associated with our business and periodic updates to such risks, and reports to our Board of Directors regarding these activities.

Stockholder Communications to the Board of Directors

Generally, stockholders who have questions or concerns should contact our Investor Relations department at 857-242-1547 or ir@sperotherapeutics.com. However, any stockholders who wish to address questions regarding our business directly with the Board of Directors, or any individual director, should direct his or her questions in writing to the Chairman of the Board of Directors at Spero Therapeutics, Inc., 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts 02139. Communications will be distributed to the Board of Directors, or to any individual director or directors as appropriate, depending on the facts and circumstances outlined in the communications. Items that are unrelated to the duties and responsibilities of the Board of Directors may be excluded, such as:

- junk mail and mass mailings
- resumes and other forms of job inquiries
- surveys
- solicitations or advertisements

In addition, any material that is unduly hostile, threatening, or illegal in nature may be excluded, provided that any communication that is filtered out will be made available to any outside director upon request.

Executive Officers

The following table sets forth certain information regarding our executive officers who are not also directors. We have employment agreements or consulting agreements with each of our executive officers.

Name	Age	Position
Stephen J. DiPalma	61	Chief Financial Officer (Interim)
Cristina Larkin	49	Chief Operating Officer
David Melnick, M.D.	68	Chief Medical Officer
Thomas Parr Jr., Ph.D.	66	Chief Scientific Officer
Timothy Keutzer	52	Chief Development Officer

On September 4, 2019, Mr. Joel Sendek notified us of his resignation as as the Company's Chief Financial Officer to pursue another opportunity closer to his home. Mr. Sendek's resignation was effective on November 8, 2019. Mr. Sendek's resignation was not as a result of any disagreement with our Board of Directors or any matter related to our operations, product candidates, policies or practices.

Stephen J. DiPalma has served as our interim Chief Financial Officer and Treasurer since November 2019. He is a Managing Director of Danforth Advisors, LLC, a financial consultancy that specializes in working with life sciences companies. Prior to and during his tenure at Danforth, Mr. DiPalma has served as interim Chief Financial Officer to several public and emerging companies in various stages of development. Mr. DiPalma joined Danforth in 2014 and served as Chief Financial Officer at Forum Pharmaceuticals from 2009 to 2014. He holds a B.S. from the University of Massachusetts and M.B.A. from Babson College.

Cristina Larkin has served as our Chief Operating Officer since September 2017 and had previously served as our Chief Commercial Officer since March 2016. Ms. Larkin has over 26 years of experience developing strategic commercial insights for biopharmaceutical companies and their infectious disease products such as Avycaz®, Dalvance®, Teflaro®, Levaquin® and Floxin®. Prior to joining us, Ms. Larkin founded CLC Insights, LLC. Prior to that, since 2004, she worked at Actavis, plc, formerly Forest Laboratories, Inc., where she served in various positions, including Assistant Vice President from 2014 to 2015. During that time, Ms. Larkin led the commercial hospital antibiotic franchise team and was responsible for the U.S. launch and execution strategy for several antibiotics. Additionally, she was a member of the business assessments and business development team and played an integral role in several strategic ventures, including the out-licensing of ceftaroline to AstraZeneca plc and the acquisition of Durata. From 1996 to 2002, Ms. Larkin served in various roles at Ortho-McNeil Pharmaceutical, LLC. Ms. Larkin received a bachelor's degree from Florida State University.

David Melnick, M.D. has served as our Chief Medical Officer since January 2018. Prior to joining Spero, Dr. Melnick served as Vice President of Clinical Development for Anti-Infectives at Allergan since 2015. In that capacity, he oversaw the development and regulatory approval of Teflaro®, Avycaz®, and Dalvance® in the United States. Prior to Allergan, Dr. Melnick served fifteen years at AstraZeneca in various levels of increasing responsibility, most recently as Vice President of Clinical Development for Anti-Infectives. In that capacity, he oversaw the late stage clinical development of Merrem®, Teflaro®, and Avycaz®. In addition, he served as the acting Vice President for early development at AstraZeneca. He received his medical training at Columbia University, followed by a Residency in Internal Medicine at The New York Hospital-Cornell Medical Center. Following a Fellowship in Infectious Disease at Yale University, he held faculty positions at the Boston University School of Medicine and the National Institute of Allergy and Infectious Diseases. He subsequently joined Kaiser-Permanente as a practicing Infectious Diseases specialist and as the Director of HIV Clinical Research at Kaiser Permanente Mid-Atlantic, with a faculty appointment at Georgetown University.

Thomas Parr Jr., Ph.D. has served as our Chief Scientific Officer since April 2014. He has more than 30 years of drug discovery experience across both large pharmaceutical and small biotechnology companies. Prior to joining Spero, from 2012 to 2014, Dr. Parr was the Chief Scientific Officer at Fedora Pharmaceuticals, Inc. where the company moved novel diazabicyclooctane beta-lactramase inhibitors toward development partnerships. Prior to Fedora, he was the Chief Scientific Officer at Targanta Therapeutics, now part of The Medicines Company. Dr. Parr earned his Ph.D. from the University of Calgary and conducted a postdoctoral fellowship at the University of British Columbia. He was an Assistant Professor in the Department of Microbiology and Biochemistry at the University of Ottawa before beginning his drug discovery and development career.

Timothy Keutzer has served as our Chief Development Officer since June 2019. He has over 20 years experience in the pharmaceutical industry, spanning multiple functional and therapeutic areas. Prior to joining Spero, Mr. Keutzer served in various roles at Cubist Pharmaceuticals, including Vice President of Program and Portfolio Management from May 2014 to July 2015. At Cubist Mr. Keutzer was the program leader for ceftolozane/tazobactam, which progressed rapidly from Phase 1 to Phase 3, and was approved in the FDA in December of 2014. Prior to that role, he also led several of Cubist's in-licensed development programs, and also led the commercial supply chain for Cubicin. His experience before Cubist spans multiple drug classes, and includes preclinical PK/PD and clinical operations at Genetics Institute, as well as global strategic marketing and program management at Wyeth. Tim began his career in contract toxicology labs. Mr. Keutzer earned his bachelor's degree from the University of Kentucky.

Item 11. Executive Compensation.

Summary Compensation Table

The following table shows the total compensation paid or accrued during the last two fiscal years ended December 31, 2019 and 2018 to our President and Chief Executive Officer and our two next most highly compensated executive officers who earned more than $100,000 during the fiscal year ended December 31, 2019 and were serving as executive officers as of such date.

Name and Principal Position	Year	Salary ($)	Bonus ($) (1)	Stock Awards ($)(2)	Option Awards ($)(3)	Non-Equity Incentive Plan Compensation ($)(4)	All other Compensation ($)(5)	Total ($)
Ankit Mahadevia, M.D.	2019	497,083	—	285,023	752,778	250,000	792	1,785,676
Chief Executive Officer	2018	465,000	—	—	—	255,750	574	721,324
Christina Larkin	2019	394,167	—	118,493	271,837	158,000	792	943,289
Chief Operating Officer	2018	385,000	—	—	—	148,225	574	533,799
David Melnick, M.D.	2019	389,167	—	118,493	271,837	156,000	792	936,288
Chief Medical Officer	2018	375,680	10,000	—	1,082,146	146,300	20,235	1,634,361

(1) Consists of a sign-on bonus to Dr. Melnick in connection with his commencement of employment in January 2018.

(2) These amounts represent the aggregate grant date fair value for performance-based stock awards computed in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, or ASC 718. A discussion of the assumptions used in determining grant date fair value may be found in Note 9 to our consolidated financial statements for the year ended December 31, 2019.

(3) These amounts represent the aggregate grant date fair value for option awards computed in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, or ASC 718. A discussion of the assumptions used in determining grant date fair value may be found in Note 9 to our consolidated financial statements for the year ended December 31, 2019.

(4) Amounts represent cash bonuses earned for the applicable fiscal year.

(5) Consists of the dollar value of life insurance premiums the Company paid with respect to term life insurance for the benefit of the executive officers named in the table above. With respect to Dr. Melnick, this amount also includes the reimbursement of certain relocation expenses in the amount of $19,661 paid in 2018.

Narrative Disclosure to Summary Compensation Table

Our employment arrangements with our named executive officers are described below.

Ankit Mahadevia, M.D.

On March 2, 2015, Dr. Mahadevia executed an offer letter with respect to his employment as our Chief Executive Officer beginning on the same date. Under the terms of the offer letter, Dr. Mahadevia's annual base salary was $360,500 in 2016 and $400,000 effective on May 19, 2017. Under the offer letter, he was eligible to receive an annual incentive bonus determined at the discretion of our Board of Directors or Compensation Committee, with a target bonus opportunity of 30% of his then-current base salary.

Dr. Mahadevia entered into a new employment agreement on October 20, 2017. This agreement provides for the following increased severance payments upon termination by us without Cause (as defined below) or by Dr. Mahadevia for Good Reason (as defined below): (i) payment of his then-current base salary for a period of 12 months following termination; (ii) a pro-rated target bonus for the period during which Dr. Mahadevia was employed in the year of termination; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date Dr. Mahadevia becomes eligible for medical benefits with another employer. Further, the new agreement provides that upon termination by us without Cause or by Dr. Mahadevia for Good Reason within 90 days prior to the earlier to occur of a Change of Control (as defined below) or the execution of a definitive agreement the consummation of which would result in a Change of Control or one year following a Change of Control (a "Change of Control Termination"), Dr. Mahadevia will be entitled to receive (i) a lump sum payment equal to 12 months of his then-current base salary plus a pro-rated target bonus for the period during which Dr. Mahadevia was employed in the year of termination; (ii) acceleration of all unvested equity awards as of the date of termination; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date Dr. Mahadevia becomes eligible for medical benefits with another employer. Payment in each case is subject to Dr. Mahadevia's execution of a release satisfactory to us following such termination.

In addition, if Dr. Mahadevia's employment terminates as a result of disability or death, he shall be entitled to receive a pro-rated target bonus for the period during which Dr. Mahadevia was employed in the year of termination. The new agreement also provides that Dr. Mahadevia shall serve as a member of our Board of Directors during his employment with us until the term of his directorship expires and he is not re-elected or his earlier resignation or removal from our Board of Directors.

In December 2017, Dr. Mahadevia's base salary was increased, effective January 1, 2018, to $465,000 with a target bonus opportunity of 50% of base salary. In December 2018, Dr. Mahadevia's base salary was increased, effective February 1, 2019, to $500,000 with a target bonus opportunity of 50% of his base salary. In December 2019, Dr. Mahadevia's base salary was increased, effective February 1, 2020, to $540,000, with a target bonus opportunity of 50% of his base salary.

David Melnick, M.D.

On December 13, 2017, we entered into an agreement with Dr. Melnick with respect to his employment as our Chief Medical Officer commencing on January 4, 2018. The terms of Mr. Melnick's offer letter provided for an annual base salary of $380,000 prorated for fiscal year 2018, and eligibility for an annual incentive bonus, with a target bonus opportunity of 35% of his then-current base salary. In December 2018, Dr. Melnick's base salary was increased, effective February 1, 2019, to $390,000 with a target bonus opportunity of 40% of base salary. In addition, Dr. Melnick was granted an option to purchase 135,000 shares of common stock and received a sign-on bonus of $10,000. In December 2019, Dr. Melnick's base salary was increased, effective February 1, 2020, to $413,400 with a target bonus opportunity of 40% of his base salary.

The agreement also provides for the following severance payments upon termination by us without Cause or by Dr. Melnick for Good Reason: (i) payment of his then-current base salary for a period of nine months following termination; (ii) a pro-rated target bonus for the period during which Dr. Melnick was employed in the year of termination; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date Dr. Melnick becomes eligible for medical benefits with another employer. Further, the agreement provides that upon termination by us without Cause or by Dr. Melnick for Good Reason within 90 days prior to the earlier to occur of a Change of Control or the execution of a definitive agreement the consummation of which would result in a Change of Control or one year following a Change of Control (a "Change of Control Termination"), Dr. Melnick will be entitled to receive: (i) a lump sum payment equal to 12 months of his then-current base salary plus a pro-rated target bonus for the period during which Dr. Melnick was employed in the year of termination; (ii) acceleration of (A) all unvested equity awards as of the date of termination if Dr. Melnick's employment commenced at least 24 months prior to a Change of Control (B) 50% of all unvested equity awards as of the date of termination if Melnick's employment commenced fewer than 24 months but at least 12 months prior to a Change of Control and (C) 25% of all unvested equity awards as of the date of termination if Dr. Melnick's employment commenced fewer than 12 months prior to a Change of Control; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date Dr. Melnick becomes eligible for medical benefits with another employer. Payment in each case is subject to Dr. Melnick's execution of a release satisfactory to us following such termination. In addition, if Dr. Melnick's employment terminates as a result of disability or death, he shall be entitled to receive a pro-rated target bonus for the period during which Dr. Melnick was employed in the year of termination.

Cristina Larkin

In February 2016, Cristina Larkin, our then Chief Commercial Officer, executed an offer letter with respect to her employment beginning on March 7, 2016. In September 2017 Ms. Larkin was promoted to Chief Operating Officer, in connection with which her bonus target was increased from 25% to 30% of her then-current base salary. In October 2017, we entered into a new employment agreement with Ms. Larkin, which provided for a base salary of $345,000 and eligibility for an annual incentive bonus, with a target bonus opportunity of 30% of her then-current base salary. In December 2017, Ms. Larkin's base salary was increased, effective January 1, 2018, to $385,000 with a target bonus opportunity of 35% of base salary. In December 2018, Ms. Larkin's base salary was increased, effective February 1, 2019, to $395,000 with a target bonus opportunity of 40% of base salary. In December 2019, Ms. Larkin's base salary was increased, effective February 1, 2020, to $404,875 with a target bonus opportunity of 40% of her base salary.

The agreement also provides for the following severance payments upon termination by us without Cause or by Ms. Larkin for Good Reason: (i) payment of her then-current base salary for a period of nine months following termination; (ii) a pro-rated target bonus for the period during which Ms. Larkin was employed in the year of termination; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date Ms. Larkin becomes eligible for medical benefits with another employer. Further, the agreement provides that upon termination by us without Cause or by Ms. Larkin for Good Reason within 90 days prior to the earlier to occur of a Change of Control or the execution of a definitive agreement the consummation of which would result in a Change of Control or one year following a Change of Control (a "Change of Control Termination"), Ms. Larkin will be entitled to receive: (i) a lump sum payment equal to 12 months of her then-current base salary plus a pro-rated target bonus for the period during which Ms. Larkin was employed in the year of termination; (ii) acceleration of (A) all unvested equity awards as of the date of termination if Ms. Larkin's employment commenced at least 24 months prior to a Change of Control (B) 50% of all unvested equity awards as of the date of termination if Ms. Larkin's employment commenced fewer than 24 months but at least 12 months prior to a Change of Control or (C) 25% of all unvested equity awards as of the date of termination if Ms. Larkin's employment commenced fewer than 12 months prior to a Change of Control; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date Ms. Larkin becomes eligible for medical benefits with another employer. Payment in each case is subject to Ms. Larkin's execution of a release satisfactory to us following such termination. In addition, if Ms. Larkin's employment terminates as a result of disability or death, she shall be entitled to receive a pro-rated target bonus for the period during which Ms. Larkin was employed in the year of termination.

Under each of the employment agreements, Cause means (i) the executive's conviction of (A) a felony or (B) any misdemeanor involving moral turpitude, deceit, dishonesty or fraud; (ii) the executive's willful failure or refusal to comply with lawful directions of our Board of Directors, with respect to Dr. Mahadevia, or of our Chief Executive Officer, with respect to Dr. Melnick and Ms. Larkin, which failure or refusal continues for more than thirty days after written notice is given to the executive by our Board of Directors, with respect to Dr. Mahadevia, or by our Chief Executive Officer, with respect to Dr. Melnick and Ms. Larkin, which notice sets forth in reasonable detail the nature of such failure or refusal; (iii) willful and material breach by the executive of a written company policy applicable to the executive or the executive's covenants and/or obligations under his or her employment agreement or the material breach of the executive's proprietary information and inventions assignment agreement; and/or (iv) material misconduct by the executive that seriously discredits or damages us or any of our affiliates.

Under each of the employment agreements, Good Reason means (i) relocation of the executive's principal business location to a location more than thirty (30) miles from the executive's then-current business location; (ii) a material diminution in the executive's duties, authority or responsibilities; (iii) a material reduction in the executive's base salary; (iv) willful and material breach by us of our covenants and/or obligations under the executive's employment agreement; or (v) within one year following a Change of Control, the executive is not an executive of the parent company, provided that the executive's roles responsibilities and scope of authority within the subsidiary is not comparable to the executive's roles, responsibilities and scope of authority with us prior to the Change of Control.

Under each of the employment agreements, Change of Control means (i) any person (as such term is used in Sections 13(d) and 14(d) of the Exchange Act) becomes the beneficial owner, directly or indirectly, of securities of the Company representing fifty percent (50%) or more of the total voting power represented by the Company's then outstanding voting securities (excluding for this purpose any such voting securities held by the Company, or any affiliate, parent or subsidiary of the Company, or by any employee benefit plan of the Company) pursuant to a transaction or a series of related transactions; (ii) a merger or consolidation of the Company other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or the parent of such corporation) at least fifty percent (50%) of the total voting power represented by the voting securities of the Company or such surviving entity or parent of such corporation, as the case may be, outstanding immediately after such merger or consolidation; (iii) our stockholders approve an agreement for the sale or disposition by the Company of all or substantially all of our assets; or (iv) a change in the composition of our Board of Directors, as a result of which fewer than a majority of the directors are incumbent directors.

All of our executive officers have entered into our standard proprietary information and inventions assignment agreement.

Outstanding Equity Awards at 2019 Fiscal Year-End

On June 30, 2017, we completed a series of transactions pursuant to which Spero Therapeutics, LLC merged with and into Spero Therapeutics, Inc., with Spero Therapeutics, Inc. continuing as the surviving corporation (the "2017 Reorganization"). As part of the 2017 Reorganization, each of the capital units of Spero Therapeutics, LLC issued and outstanding prior to the 2017 Reorganization was cancelled and converted into and exchanged for one share of Spero Therapeutics, Inc. capital stock of the same class and/or series, and each of the incentive units of Spero Therapeutics, LLC was terminated and cancelled. Promptly after the 2017 Reorganization, previous holders of incentive units who were still employed by us at the time of the Reorganization received stock options under the 2017 Plan. Such stock options were granted for the same number of shares of our common stock as the number of incentive units cancelled, and the stock options were granted with continued vesting on the same terms and with similar rights and restrictions as the incentive units. All such stock options have an exercise price of $5.90.

The following table shows grants of stock options outstanding on the last day of the fiscal year ended December 31, 2019 to each of the executive officers named in the Summary Compensation Table.

	Option Awards						Stock Awards				
Name	Number of Securities Underlying Unexercised Options (#) Exercisable		Number of Securities Underlying Unexercised Options (#) Unexercisable		Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have not Vested (#)	Market Value of Shares or Units of Stock that Have not Vested ($)	Equity incentive plan awards: number of unearned shares, units or other rights that have not vested		Equity incentive plan awards: market or payout value of unearned shares, units or other rights that have not vested ($)
Ankit Mahadevia, M.D.	22,213	(1)	—		$ 5.90	7/5/2027	—	—	—		—
	93,028	(2)	8,460	(2)	$ 5.90	7/5/2027	—	—	—		—
	118,888	(3)	—		$ 5.90	7/5/2027	—	—	—		—
	179,572	(4)	117,648	(4)	$ 5.90	7/5/2027	—	—	—		—
	62,539	(5)	62,540	(5)	$ 11.63	12/12/2027	—	—	—		—
	—		180,000	(6)	$ 6.26	1/1/2029	—	—	—		—
	—		43,901	(7)	$ 12.81	3/29/2029	—	—	—		—
	—		—		—	—	—	—	22,250	(8)	285,023
Cristina Larkin	18,907	(9)	1,527	(9)	$ 5.90	7/5/2027	—	—	—		—
	5,949	(10)	541	(10)	$ 5.90	7/5/2027	—	—	—		—
	42,758	(4)	28,021	(4)	$ 5.90	7/5/2027	—	—	—		—
	31,270	(5)	31,270	(5)	$ 11.63	12/12/2027	—	—	—		—
	—		65,000	(6)	$ 6.26	1/1/2029	—	—	—		—
	—		15,854	(7)	$ 12.81	3/29/2029	—	—	—		
	—		—		—	—	—	—	9,250	(8)	118,493
David Melnick, M.D.	64,688	(11)	70,312	(11)	$ 12.14	1/3/2028	—	—	—		—
	—		65,000	(6)	$ 6.26	1/1/2029	—	—	—		—
	—		15,854	(7)	$ 12.81	3/29/2029	—	—	—		—
	—		—		—	—	—	—	9,250	(8)	118,493

(1) 100% of these options vested on August 24, 2019.

(2) As part of the 2017 Reorganization, Dr. Mahadevia was granted options to replace his previously awarded incentive units in Spero Therapeutics, LLC. The options vest in accordance with the vesting terms of Dr. Mahadevia's previously held incentive units: 25% of the underlying shares were deemed vested April 28, 2017, the first anniversary of the vesting commencement date, with an additional 1/36th of the remaining shares vesting monthly thereafter until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his employment agreement.

(3) 100% of these options vested on July 6, 2017.

(4) 25% of the options vested on July 6, 2018 and an additional 1/36th of the remaining shares vest monthly until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his or her employment agreement.

(5) 25% of the options vested on December 13, 2018 and an additional 1/36th of the remaining shares vest monthly until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his or her employment agreement.

(6) 25% of the options vest on January 2, 2020 and an additional 1/36th of the remaining shares vest monthly until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his or her employment agreement.

(7) These performance-based options, which were granted in March 2019, vest in four equal installments upon the achievement, within the performance period ending December 31, 2020, of certain performance goals, which are more fully described below under "Performance-Based Equity Incentive Awards," and are contingent on the executive remaining an employee, director or consultant of Spero as of each such date.

(8) These performance-based restricted stock units, which were granted in March 2019, vest in four equal installments upon the achievement, within the performance period ending December 31, 2020, of certain performance goals, which are more fully described below under "Performance-Based Equity Incentive Awards," and are contingent on the executive remaining an employee, director or consultant of Spero as of each such date.

(9) As part of the Company's 2017 Reorganization, Ms. Larkin was granted options to replace her previously awarded incentive units in Spero Therapeutics, LLC. The options vest in accordance with the vesting terms of Ms. Larkin's previously held incentive units: 25% of the underlying shares were deemed vested on March 7, 2017, the first anniversary of the vesting commencement date, with an additional 1/36th of the remaining shares vesting monthly thereafter until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and her employment agreement.

(10) As part of the Reorganization, Ms. Larkin was granted options to replace her previously awarded incentive units in Spero Therapeutics, LLC. The options vest in accordance with the vesting terms of Ms. Larkin's previously held incentive units: 25% of the underlying shares were deemed vested April 28, 2017, the first anniversary of the vesting commencement date, with an additional 1/36th of the remaining shares vesting monthly thereafter until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and her employment agreement.

(11) 25% of the options vested on January 4, 2019 and an additional 1/36th of the remaining shares vest monthly until the option is fully vested. In addition, in the event of a Change of Control Termination, the vesting of these options will accelerate in accordance with the terms of the option and his employment agreement.

Performance-Based Equity Incentive Awards

Historically, we have generally granted stock options with time-based vesting to our executives at the time of hire and on an annual basis thereafter. In March 2019, in addition to the foregoing, we granted an aggregate of 150,000 performance-based options and restricted stock units ("RSUs") to our senior executives. These options and RSUs (the "Performance Awards") are subject to performance-based vesting eligibility and a subsequent partial time-based vesting schedule. Specifically, the Performance Awards are eligible for vesting based on the achievement of performance criteria, each representing a 25% vesting opportunity if achieved within a specified time during the performance period (the "Performance Period"), and relating to (i) the release of tebipenem HBr top-line data; (ii) FDA acceptance of a tebipenem HBr New Drug Application; (iii) non-dilutive financing; and (iv) equity financing. Following the Performance Period, Performance Awards determined to be eligible for vesting as a result of achievement of the performance criteria will vest as follows: (a) 50% of the eligible award will vest immediately, and (b) the remaining eligible award will vest (i) in the case of options, in equal monthly instalments ending two years after the Performance Period expiration, and (ii) in the case of RSUs, on such two year anniversary. The Performance Awards will be subject to provisions of the executives' employment agreements regarding acceleration of vesting in the event of certain termination events following a change in control only to the extent previously determined to be eligible for vesting as a result of achievement of the performance criteria. We believe the achievement of the performance criteria will require significant execution and effort by the executives with no assurance of achievement guaranteed. Awards for which the performance criteria has not been achieved as specified during the Performance Period will lapse.

Potential Payments upon Termination or Change-In-Control

The employment agreements provide for the following severance payments upon termination by us without Cause or by the employee for Good Reason: (i) payment of the employee's then-current base salary for a period of nine months following termination (12 months in the case of the Chief Executive Officer); (ii) a pro-rated target bonus for the period during which the employee was employed in the year of termination; and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date the employee becomes eligible for medical benefits with another employer.

Further, the agreements provide that upon termination by us without Cause or by the employee for Good Reason within 90 days prior to or one year following the earlier to occur of a Change of Control (as defined in the executive's employment agreements) or the execution of a definitive agreement the consummation of which would result in a Change of Control, the employee will be entitled to receive: (i) a lump sum payment equal to 12 months of the employee's then-current base salary plus a pro-rated target bonus for the period during which the employee was employed in the year of termination; (ii) acceleration of unvested equity awards as of the date of termination in accordance with the terms of the executive's employment agreement, as described above under "Narrative Disclosure to Summary Compensation Table;" and (iii) continued coverage under our group health insurance plan until the earlier of 12 months from termination or the date the employee becomes eligible for medical benefits with another employer. Payment in each case is subject to the employee's execution of a release satisfactory to us following such termination. In addition, if the employee's employment terminates as a result of disability or death, he or she shall be entitled to receive a pro-rated target bonus for the period during which the employee was employed in the year of termination.

Director Compensation

The following table shows the total compensation paid or accrued during the fiscal year ended December 31, 2019 to each of our current and former non-employee directors. Cynthia Smith joined our Board of Directors in March 2019. Directors who are employed by us are not compensated for their service on our Board of Directors.

Name	Fees Earned or Paid in Cash ($)	Option Awards* ($)(5)	Total($)
Milind Deshpande, Ph.D.	77,500	45,374(3)	122,874
Jean-François Formela, M.D.	44,000	45,374(3)	89,374
John C. Pottage, Jr., M.D.	52,500	45,374(3)	97,874
Cynthia Smith(1)	31,264	151,135(3)(4)	182,399
David P. Southwell(2)	10,625	—	10,625
Frank E. Thomas	54,000	45,374(3)	99,374
Patrick Vink, M.D.	52,500	45,374(3)	97,874

* These amounts represent the aggregate grant date fair value of options granted to each director in the fiscal year ended December 31, 2019, computed in accordance with FASB ASC Topic 718. A discussion of the assumptions used in determining grant date fair value may be found in Note 9 to our consolidated financial statements, included in this Annual Report on Form 10-K..

(1) Ms. Smith joined our Board of Directors in March 2019.

(2) Mr. Southwell resigned from our Board of Directors in April 2019.

(3) Represents an option to purchase 6,073 shares of common stock at an exercise price of $10.67. The shares underlying the option award vest and become fully exercisable on June 5, 2020, subject to the individual's continued service as of such date.

(4) Represents an option to purchase 12,146 shares of common stock at an exercise price of $12.81. The shares underlying the option award vest in thirty-six equal monthly installments at the end of each successive month following March 29, 2019, subject to the individual's continued service as of such date.

(5) As of December 31, 2019, the aggregate number of options held by each of our non-employee directors was as follows (representing both exercisable and unexercisable option awards, none of which have been exercised):

Name	Number of Shares Underlying Outstanding Stock Options
Milind Deshpande, Ph.D.	60,627
Jean François Formela, M.D.	12,146
John C. Pottage, Jr., M.D.	18,219
Cynthia Smith	18,219
Frank E. Thomas	42,661
Patrick Vink, M.D.	42,660

Non-Employee Director Compensation Policy

Under our Non-Employee Director Compensation Policy, as amended, each non-employee director is eligible to receive compensation for his or her service consisting of annual cash retainers and equity awards. Our non-employee directors receive the following annual retainers for their service:

Position	Retainer
Board Member	$ 35,000
Board Chairperson (additional retainer)	30,000
Lead Director, if any (additional retainer)	18,750
Audit Committee Chair	15,000
Compensation Committee Chair	10,000
Nominating and Governance Committee Chair	7,500
Audit Committee Member	7,500
Compensation Committee Member	5,000
Nominating and Governance Committee Member	4,000

In December 2019 we amended our Non-Employee Director Compensation Policy to provide the following with respect to equity awards to non-employee directors: (i) the initial equity award consisting of a non-qualified stock option to purchase shares of our common stock upon first appointment to our Board of Directors and vesting in equal monthly installments until the third anniversary of the grant date was increased from 12,146 shares to 15,000 shares, subject to the non-employee director's continued service, and (ii) annual equity awards commencing in 2018 consisting of a non-qualified stock option to purchase shares of our common stock vesting on the first anniversary of the grant date was increased from 6,073 shares to 7,500 shares, subject to the non-employee director's continued service. The policy was further amended to provide that, prior to the beginning of each calendar year, a non-employee director may elect to receive all or a portion of his or her base annual fee for service on our Board of Directors (i.e., $35,000) in the form of a non-qualified stock option to purchase the number of shares of our common stock as is equal to the Black-Scholes value of such fee (or portion thereof), which option will be granted on the first business day of the calendar year.

Directors may be reimbursed for travel, food, lodging and other expenses directly related to their service as directors. Directors are also entitled to the protection provided by their indemnification agreements and the indemnification provisions in our amended and restated certificate of incorporation and amended and restated By-Laws.

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

The following table sets forth certain information with respect to the beneficial ownership of our common stock as of March 1, 2020 for (a) the executive officers named in the Summary Compensation Table on Item 11 of this Annual Report on Form 10-K, (b) each of our directors and director nominees, (c) all of our current directors and executive officers as a group and (d) each stockholder known by us to own beneficially more than 5% of our common stock. Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to the securities. We deem shares of common stock that may be acquired by an individual or group within 60 days of March 1, 2020 pursuant to the exercise of options to be outstanding for the purpose of computing the percentage ownership of such individual or group, but not outstanding for the purpose of computing the percentage ownership of any other person shown in the table. Except as indicated in footnotes to this table, we believe that the stockholders named in this table have sole voting and investment power with respect to all shares of common stock shown to be beneficially owned by them based on information provided to us by these stockholders. Percentage of ownership is based on 19,190,695 shares of common stock outstanding on December 31, 2019.

Name of Beneficial Owner	Number of Shares Beneficially Owned	Percent of Shares Beneficially Owned
Principal Stockholders		
S.R. One, Limited (1)	1,934,006	10.08%
Entities affiliated with BVF Inc. (2)	2,028,405	9.99%
Atlas Venture Fund IX, L.P. (3)	1,376,968	7.18%
GV 2015, L.P. (4)	1,112,473	5.80%
Entities affiliated with Aquilo Capital Management, LLC (5)	1,154,356	6.02%
Atlas Venture Fund X, LLC (6)	1,031,160	5.37%
Named Executive Officers and Directors		
Ankit Mahadevia, M.D. (7)	644,517	3.36%
Cristina Larkin (8)	137,738	*
David Melnick, M.D. (9)	96,251	*
Milind Deshpande, Ph.D. (10)	58,238	*
Jean-François Formela, M.D. (11)	1,986,982	10.35%
John C. Pottage, Jr., M.D. (12)	6,073	*
Cynthia Smith (13)	4,048	*
Frank E. Thomas (14)	27,728	*
Patrick Vink, M.D. (15)	31,203	*
All current executive officers and directors as a group (11 persons) (16)	3,208,772	16.72%

* Indicates beneficial ownership of less than 1%.

(1) Consists of 1,934,006 shares of common stock owned by S.R. One, Limited, or S.R. One, an indirect wholly owned subsidiary of GlaxoSmithKline plc. The address for S.R. One is 161 Washington Street, Suite 500, Eight Tower Bridge, Conshohocken, Pennsylvania 19428. This information is based solely on a Schedule 13D/A filed by GlaxoSmithKline plc with the SEC on February 14, 2020, which reported ownership as of such date.

(2) Includes (i) 1,217,924 shares of common stock held by Biotechnology Value Fund, L.P., or BVF, (ii) 664,230 shares of common stock held by Biotechnology Value Fund II, L.P., or BVF II, and (iii) 55,550 shares of common stock held by Biotechnology Value Trading Fund OS LP, or Trading Fund OS. BVF I GP LLC, or BVF GP, as general partner of BVF, may be deemed to beneficially own 1,217,924 shares of common stock beneficially owned by BVF. BVF II GP LLC, or BVF II GP, as general partner of BVF II, may be deemed to beneficially own 664,230 shares of common stock beneficially owned by BVF II. BVF Partners OS Ltd, or Partners OS, as general partner of Trading Fund OS, may be deemed to beneficially own 55,550 shares of common stock beneficially owned by Trading Fund OS. BVF GP Holdings LLC, or BVF GPH, as the sole member of BVF GP and BVF II GP, may be deemed to beneficially own 1,882,154 shares of common stock beneficially owned in the aggregate by BVF GP and BVF II GP. BVF Partners L.P., or Partners, as investment manager of BVF, BVF II andTrading Fund OS, and the sole member of Partners OS, may be deemed to beneficially own the 2,028,405 shares of common stock beneficially owned in the aggregate by BVF, BVF II, Trading Fund OS, and certain managed accounts of Partners, or the Partners Managed Accounts, including 90,701 shares of common stock held in the Partners Managed Accounts. BVF Inc., as the general partner of Partners, may be deemed to beneficially own the 2,028,405 shares of common stock owned by Partners. Mark N. Lampert is a director and officer of BVF Inc., and may be deemed to beneficially own the 2,028,405 shares of common stock beneficially owned by BVF, Inc. Together, BVF, BVF II, BVF GP, BVF II GP, Trading Fund OS, BVF GPH, Partners OS, Partners, BVF Inc. and Mark N. Lampert (the "BVF Entities") hold 1,720 shares of Series A Convertible Preferred Stock ("Series A Preferred") convertible for an aggregate of 1,720,000 shares of common stock. The Series A Preferred may not be converted if, after such conversion, the BVF Entities would beneficially own more than 9.99% of the common stock then issued and outstanding (the "Series A Blocker"). As of December 31, 2019, the Series A Blocker limited the aggregate conversion of Series A Preferred to 1,183,000 of the 1,720,000 shares of common stock underlying the Series A Preferred. As a result of the Series A Blocker, included in the percentage of shares beneficially owned as of December 31, 2019 is the maximum number of shares of common stock issuable upon conversion of Series A Preferred up to the limit imposed by the Series A Blocker, and excluded are the remaining shares of common stock issuable upon conversion of Series A Preferred that are prevented from converting due to the Series A Blocker. Together the BVF Entities also hold 1,000 shares of Series B Convertible Preferred Stock (the "Series B Preferred") convertible for an aggregate of 1,000,000 shares of common stock. The Series B Preferred may not be converted if, after such conversion, the BVF Entities would beneficially own more than 9.99% of the common stock then issued and outstanding (the "Series B Blocker"). As of December 31, 2019, the Series B Blocker limits the aggregate conversion of Series B Preferred by the BVF Entities to 0 out of the 1,000,000 shares of common stock underlying the Series B Preferred. BVF GP disclaims beneficial ownership of the shares of common stock beneficially owned by BVF. BVF II GP disclaims beneficial ownership of the shares of common stock beneficially owned by BVF II. Partners OS disclaims beneficial ownership of the shares of common stock beneficially owned by Trading Fund OS. BVF GPH disclaims beneficial ownership of the shares of common stock beneficially owned by BVF GP and BVF II GP. Each of Partners, BVF Inc. and Mr. Lampert disclaims beneficial ownership of the shares of common stock beneficially owned by BVF, BVF II, Trading Fund OS, and the Partners Management Accounts. The address of the principal business and office of BVF Inc. and certain of its affiliates is 1 Sansome Street, 30th Floor, San Francisco, California, 94194. This information is based solely on a Schedule 13G/A filed with the SEC on February 18, 2020, which reported ownership as of December 31, 2019.

(3) All shares are held directly by Atlas Venture Fund IX. Atlas Venture Associates IX, L.P., or AVA IX LP, is the general partner of Atlas Venture Fund IX, and Atlas Venture Associates IX, LLC, or AVA IX LLC, is the general partner of AVA IX LP. Peter Barrett, Bruce Booth, Jean-François Formela, M.D., Jeff Fagnan, and Ryan Moore are the members of AVA IX LLC and collectively make investment decisions on behalf of Atlas Venture Fund IX. Dr. Formela is also a member of our Board of Directors. Dr. Formela disclaims beneficial ownership of such shares of common stock, except to the extent of his pecuniary interest therein, if any. The address for Atlas Venture Fund IX, is 25 First Street, Suite 303, Cambridge, Massachusetts 02141. This information is based solely on a Schedule 13G/A filed by Atlas Venture Fund IX, L.P. with the SEC on February 4, 2020, which reported ownership as of December 31, 2019.

(4) GV 2015 GP, L.L.C., the general partner of GV 2015, L.P., Alphabet Holdings LLC, the sole member of GV 2015 GP, L.L.C., Google LLC, the sole member of Alphabet Holdings LLC, XXVI Holdings Inc., the managing member of Google LLC, and Alphabet Inc., the sole stockholder of XXVI Holdings Inc., may be deemed to have sole power to vote or dispose of the shares held by GV 2015, L.P. The address for GV 2015, L.P., GV 2015 GP, L.L.C., Alphabet Holdings LLC, Google LLC, XXVI Holdings Inc. and Alphabet Inc. is 1600 Amphitheatre Parkway, Mountain View, California 94043. This information is based solely on a Schedule 13G filed by GV 2015, L.P. with the SEC on February 14, 2018, which reported ownership as of December 31, 2017.

(5) Aquilo Capital Management, LLC is an investment advisor that serves as the general partner and investment manager to each of Aquilo Capital, L.P. and Aquilo Capital II, L.P., (collectively, the "Aquilo Funds"), and may be deemed to be the beneficial owner of all shares of common stock held by the Aquilo Funds. Mr. Marc Schneidman, as Managing Member of Aquilo Capital Management, LLC, with the power to exercise investment and voting discretion, may be deemed to be the beneficial owner of all shares of common stock held by the Aquilo Funds. Each of the Aquilo Funds and Mr. Schneidman expressly disclaims beneficial ownership over any of the shares of common stock held by the Aquilo Funds. The address for Aquilo Capital, L.P. and Aquilo Capital II, L.P. is One Letterman Drive, Suite D4900, Building D, The Presidio, San Francisco, California 94129. This information is based solely on a Schedule 13G/A filed by Aquilo Capital, L.P. with the SEC on February 14, 2020, which reported ownership as of such date.

(6) All shares are held directly by Atlas Venture Fund X, LLC, or Atlas Fund X. Atlas Venture Associates X, L.P., or AVA X LP, is the general partner of Atlas Venture Fund X, and Atlas Venture Associates X, LLC, or AVA X LLC, is the general partner of AVA X LP. Peter Barrett, Bruce Booth, Jean-François Formela, M.D., David Gragzel and Jason Rhodes are the members of AVA X LLC and collectively make investment decisions on behalf of Atlas Venture Fund X. Dr. Formela is also a member of our Board of Directors. Dr. Formela disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest therein, if any. The address for Atlas Venture Fund X, is 400 Technology Square, 10th Floor, Cambridge, Massachusetts 02139. This information is based solely on a Schedule 13D filed by Atlas Venture Fund X, L.P. with the SEC on March 14, 2018, which reported ownership as of December 31, 2017.

(7) Consists of (i) 65,817 shares of common stock held by Mahadevia-Mehta Family Trust, of which Dr. Mahadevia is the trustee, and (ii) 578,700 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date held by Dr. Mahadevia.

(8) Consists of (i) 1,500 shares of common stock and (ii) 136,238 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date held by Ms. Larkin.

(9) Consists of 96,251 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date held by Dr. Melnick.

(10) Consists of (i) 16,454 shares of common stock and (ii) 41,784 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date held by Dr. Deshpande.

(11) See footnotes 3 and 6. Also includes 7,425 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date held by Dr. Formela.

(12) Consists of 6,073 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date held by Dr. Pottage.

(13) Consists of 4,048 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date held by Ms. Smith.

(14) Consists of 27,728 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date held by Mr. Thomas.

(15) Consists of 31,203 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date held by Dr. Vink.

(16) See notes 3, 6 and 7 through 15 above; also includes Stephen DiPalma, Thomas Parr Jr., Ph.D. and Timothy Keutzer, who are executive officers but not named executive officers.

Equity Compensation Plan Information

The following table provides certain aggregate information with respect to all of the Company's equity compensation plans in effect as of December 31, 2019:

	(a)	(b)	(c)
Plan category	**Number of securities to be issued upon exercise of outstanding options, warrants and rights (#)**	**Weighted-average exercise price of outstanding options, warrants and rights ($)**	**Number of securities remaining for future issuance under equity compensation plans (excluding securities reflected in column (a)) (#)**
Equity compensation plans approved by stockholders(1)	2,829,678	$7.94	329,457(3)
Equity compensation plans not approved by stockholders(2)	171,300	$11.42	160,200
Total:	3,000,978	$8.13	489,657

(1) This plan category consists of the Company's 2017 Stock Inventive Plan.

(2) This plan category consists of the Company's 2019 Inducement Equity Incentive Plan.

(3) Under the Company's 2017 Stock Inventive Plan, the number of shares of common stock that may be issued automatically increases on an annual basis on the first day of each fiscal year, beginning with the fiscal year until and including the fiscal year ending December 31, 2027, by an amount equal to the lesser of (i) 607,324 shares of common stock, (ii) 4% of the number of outstanding shares of our common stock on such date, or (iii) an amount determined by our Board of Directors or Compensation Committee.

Benefits Programs

Each named executive employee is eligible to participate in our benefits programs, which include health, life, disability and dental insurance and a 401(k) retirement savings plan.

Spero Therapeutics, Inc.'s 2017 Stock Incentive Plan

We adopted the Spero Therapeutics, Inc. 2017 Stock Incentive Plan on June 28, 2017, as amended on October 18, 2017 (the "2017 Plan"). The 2017 Plan will expire on June 30, 2027. Under the 2017 Plan, we may grant incentive stock options, non-qualified stock options, restricted and unrestricted stock awards and other stock-based awards.

Since its adoption, there have been 3,911,049 shares of our common stock authorized for issuance under the 2017 Plan, which amount includes the automatic increase effective as of January 1, 2020. As of March 1, 2020, a total of 227,721 shares are available for future grant under the 2017 Plan.

Our Board of Directors is authorized to administer the 2017 Plan. In accordance with the provisions of the 2017 Plan, our Board of Directors determines the terms of the options and other awards issued pursuant thereto, including the following:

- which employees, directors and consultants shall be granted awards;
- the number of shares of common stock subject to options and other awards;
- the exercise price of each option, which generally shall not be less than fair market value of the common stock on the date of grant;
- the termination or cancellation provisions applicable to the options;
- the terms and conditions of other awards, including conditions for repurchase, termination or cancellation, issue price and repurchase price; and
- all other terms and conditions upon which each award may be granted in accordance with the 2017 Plan.

No participant may receive awards for more than 1,000,000 shares of our common stock in any fiscal year.

In addition, our Board of Directors or any committee to which our Board of Directors delegates authority may, with the consent of the affected plan participants, amend outstanding awards consistent with the terms of the 2017 Plan.

Upon a merger, consolidation, or sale of all or substantially all of our assets, our Board of Directors or any committee to which our Board of Directors delegates authority, or the Board of Directors of any corporation assuming the our obligations, may, in its sole discretion, take any one or more of the following actions pursuant to the 2017 Plan, as to some or all outstanding awards, to the extent not otherwise agreed under any individual agreement:

- provide that outstanding options will be assumed or substituted for options of the successor corporation;
- provide that the outstanding options must be exercised within a certain number of days, either to the extent the options are then exercisable, or at our Board of Directors' discretion, any such options being made partially or fully exercisable;
- terminate outstanding options in exchange for a cash payment of an amount equal to the difference between (a) the consideration payable upon consummation of the corporate transaction to a holder of the number of shares into which such option would have been exercisable to the extent then exercisable, or in our Board of Directors' discretion, any such options being made partially or fully exercisable, and (b) the aggregate exercise price of those options;
- provide that outstanding stock grants will be substituted for shares of the successor corporation or consideration payable with respect to our outstanding stock in connection with the corporate transaction; and
- terminate outstanding stock grants in exchange for payment of an amount equal to the consideration payable upon consummation of the corporate transaction to a holder of the same number of shares comprising the stock grant, to the extent the stock grant is no longer subject to any forfeiture or repurchase rights, or at our Board of Directors' discretion, all forfeiture and repurchase rights being waived upon the corporate transaction. For purposes of determining such payments, in the case of a corporate transaction the consideration for which, in whole or in part, is other than cash, the consideration other than cash shall be valued at the fair market value thereof as determined in good faith by our Board of Directors.

In connection with the Company's 2017 Reorganization, all outstanding incentive units issued under Spero Therapeutics, LLC's operating agreement were cancelled. Any incentive unit holders who were employees, directors or consultants of the Company at the time of the 2017 Reorganization were issued options under the 2017 Plan with continued vesting on the same schedule and the same terms as such person's incentive units.

Spero Therapeutics, Inc.'s 2019 Inducement Equity Incentive Plan

On March 11, 2019, the Board of Directors adopted Spero Therapeutics, Inc.'s 2019 Inducement Equity Incentive Plan (the "2019 Inducement Plan") and reserved 331,500 shares of our common stock to be used exclusively for grants of awards to individuals that were not previously employees or directors of the Company, as an inducement to the individual's entry into employment with the Company within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. The 2019 Inducement Plan was adopted without stockholder approval pursuant to Rule 5635(c)(4). The 2019 Inducement Plan provides for the grant of equity-based awards, including options, restricted and unrestricted stock awards, and other stock-based awards, and its terms are substantially similar to the 2017 Plan, but with such other terms and conditions intended to comply with the Nasdaq inducement award exception.

As of March 1, 2020, there were 201,800 shares outstanding and 129,700 shares available for grant under the Inducement Plan.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. The director or officer may amend or terminate the plan in limited circumstances. Our directors and executive officers may also buy or sell additional shares of our common stock outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Related Party Transactions

Except as described below and in the compensation arrangements described in Part II, Item 11 of this Annual Report on Form 10-K, in the fiscal years ended December 31, 2019 and December 31, 2018, there has not been, nor is there currently proposed, any transaction to which we are or were a party in which the amount involved exceeds the lesser of $120,000 and 1% of the average of our total assets at year-end for the last two completed fiscal years, and in which any of our current directors, executive officers, holders of more than 5% of any class of our voting securities or any of their respective affiliates or immediate family members, had, or will have, a direct or indirect material interest.

We have entered into indemnification agreements with each of our executive officers and directors. The indemnification agreements, our amended and restated certificate of incorporation and our amended and restated By-Laws require us to indemnify our directors to the fullest extent not prohibited by Delaware law. Subject to certain limitations, our amended and restated certificate of incorporation also requires us to advance expenses incurred by our directors and officers, subject to limited exceptions. We also maintain a general liability insurance policy which covers certain liabilities of directors and officers of the Company arising out of claims based on acts or omissions in their capacities as directors or officers.

Indemnification Agreements with Officers and Directors and Directors' and Officers' Liability Insurance

We have entered into indemnification agreements with each of our executive officers and directors. The indemnification agreements, our amended and restated certificate of incorporation and our amended and restated By-Laws require us to indemnify our directors to the fullest extent not prohibited by Delaware law. Subject to certain limitations, our amended and restated certificate of incorporation also requires us to advance expenses incurred by our directors and officers, subject to limited exceptions. We also maintain a general liability insurance policy which covers certain liabilities of directors and officers of the Company arising out of claims based on acts or omissions in their capacities as directors or officers.

Policies and Procedures for Related Party Transactions

We have adopted a written policy that requires all future transactions between us and any director, executive officer, holder of 5% or more of any class of our capital stock or any member of the immediate family of, or entities affiliated with, any of them, or any other related persons, as defined in Item 404 of Regulation S-K, or their affiliates, in which the amount involved is equal to or greater than the threshold amount proscribed by Item 404 of Regulation S-K, be approved in advance by our Audit Committee. Any request for such a transaction must first be presented to our Audit Committee for review, consideration and approval. In approving or rejecting any such proposal, our Audit Committee is to consider the relevant facts and circumstances available and deemed relevant to the Audit Committee, including, but not limited to, the extent of the related party's interest in the transaction, and whether the transaction is on terms no less favorable to us than terms we could have generally obtained from an unaffiliated third party under the same or similar circumstances.

Director Independence

Our Board of Directors undertook a review of the composition of our Board of Directors and independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our Board of Directors has determined that each of Milind Deshpande, Ph.D., Jean-Francois Formela, M.D., John C. Pottage, Jr., M.D., Cynthia Smith, Frank E. Thomas and Patrick Vink, M.D. would qualify as "independent" as that term is defined by Nasdaq Listing Rule 5605(a)(2). Ankit Mahadevia, M.D. would not qualify as "independent" under applicable Nasdaq Listing Rules applicable to the Board of Directors generally or to separately designated Board committees because he currently serves as our Chief Executive Officer. In making such determinations, our Board of Directors considered the relationships that each of our non-employee directors has with our company and all other facts and circumstances deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

Subject to some exceptions, Nasdaq Listing Rule 5605(a)(2) provides that a director will only qualify as an “independent director” if, in the opinion of our Board of Directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director, and that a director cannot be an “independent director” if (a) the director is, or in the past three years has been, an employee of ours; (b) a member of the director’s immediate family is, or in the past three years has been, an executive officer of ours; (c) the director or a member of the director’s immediate family has received more than $120,000 per year in direct compensation from us within the preceding three years, other than for service as a director or benefits under a tax-qualified retirement plan or non-discretionary compensation (or, for a family member, as a non-executive employee); (d) the director or a member of the director’s immediate family is a current partner of our independent public accounting firm, or has worked for such firm in any capacity on our audit at any time during the past three years; (e) the director or a member of the director’s immediate family is, or in the past three years has been, employed as an executive officer of a company where one of our executive officers serves on the compensation committee; or (f) the director or a member of the director’s immediate family is an executive officer, partner or controlling stockholder of a company that makes payments to, or receives payments from, us in an amount which, in any 12-month period during our past three fiscal years, exceeds the greater of 5% of the recipient’s consolidated gross revenues for that year or $200,000 (except for payments arising solely from investments in our securities or payments under non-discretionary charitable contribution matching programs). Additionally, in order to be considered an independent member of an audit committee under Rule 10A-3 under the Exchange Act, a member of an audit committee may not, other than in his or her capacity as a member of the audit committee, the Board of Directors, or any other committee of the Board of Directors, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the applicable company or any of its subsidiaries or otherwise be an affiliated person of the applicable company or any of its subsidiaries. To be considered an independent member of the compensation committee under Rule 10C-1 under the Exchange Act, the Board must consider and determine whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director; and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

Item 14. Principal Accounting Fees and Services.

PricewaterhouseCoopers LLP was our independent registered public accounting firm for the fiscal years ended December 31, 2019 and 2018.

The following table presents fees for professional audit services and other services rendered by PricewaterhouseCoopers LLP to the Company for the fiscal years ended December 31, 2019 and December 31, 2018:

	Fiscal Year 2019	Fiscal Year 2018
Audit Fees(1)	$ 794,000	$ 998,250
Audit-Related Fees(2)	45,000	50,000
Tax Fees(3)	29,000	62,000
All Other Fees(4)	2,800	2,800
Total	$ 870,800	$ 1,113,050

(1) Audit fees consisted of audit work performed in the preparation of financial statements, the review of the interim consolidated financial statements, and related services that are normally provided in connection with registration statements.

(2) Audit related fees consist of fees billed by PricewaterhouseCoopers LLP for assurance and related services that are reasonably related to the performance of the audit or review of our consolidated financial statements.

(3) Tax fees incurred in 2019 and 2018 consist of fees for professional services, including tax consulting and compliance performed by PricewaterhouseCoopers LLP.

(4) All other fees represent payment for access to the PricewaterhouseCoopers LLP online accounting research and financial disclosure databases.

Policy on Audit Committee Pre-Approval of Services

Consistent with SEC policies regarding auditor independence, the Audit Committee has responsibility for appointing, setting compensation and overseeing the work of our independent registered public accounting firm. In recognition of this responsibility, the Audit Committee reviews and pre-approves all audit and permissible non-audit services provided by our independent registered public accounting firm; provided, however, that de minimis non-audit services may instead be approved in accordance with applicable SEC rules.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) Consolidated Financial Statements

See Index to Consolidated Financial Statements at Item 8 herein.

(2) Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the consolidated financial statements or notes thereto.

(3) Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
3.1	Amended and Restated Certificate of Incorporation of the Registrant		Form 8-K (Exhibit 3.1)	11/6/2017	001-38266
3.2	Amended and Restated Bylaws of the Registrant		Form 8-K (Exhibit 3.2)	11/6/2017	001-38266
3.3	Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	7/17/2018	001-38266
3.4	Certificate of Designation of Preferences, Rights and Limitations of Series B Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	11/16/2018	001-38266
3.4	Certificate of Designation of Preferences, Rights and Limitations of Series C Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	2/28/2020	001-38266
4.1	Form of Common Stock Certificate		Form S-1 (Exhibit 4.1)	10/6/2017	333-220858
4.2	Investors' Rights Agreement, dated as of June 30, 2017, by and between the Registrant and the other parties thereto		Form S-1 (Exhibit 4.2)	10/6/2017	333-220858
4.3	Description of Registrant's Securities	X			
10.1#	2017 Stock Incentive Plan, as amended		Form 10-Q (Exhibit 10.1)	12/14/2017	001-38266
10.2#	Form of Stock Option Agreement under the 2017 Stock Incentive Plan, as amended		Form 10-Q (Exhibit 10.2)	12/14/2017	001-38266
10.3#	2019 Inducement Equity Incentive Plan		Form 10-K (Exhibit 10.3)	3/14/2019	001-38266
10.4#	Form of Stock Option Agreement under the 2019 Inducement Equity Incentive Plan		Form 10-K (Exhibit 10.4)	3/14/2019	001-38266
10.5#	Form of Director and Officer Indemnification Agreement		Form S-1 (Exhibit 10.4)	10/6/2017	333-220858
10.6#	Non-Employee Director Compensation Policy, as amended	X			
10.7#	Employment Agreement, dated October 20, 2017, by and between the Registrant and Ankit Mahadevia, M.D.		Form S-1/A (Exhibit 10.5)	10/23/2017	333-220858

10.8#	Employment Agreement, dated October 20, 2017, by and between the Registrant and Joel Sendek		Form S-1/A (Exhibit 10.6)	10/23/2017	333-220858
10.9#	Employment Agreement, dated October 20, 2017, by and between the Registrant and Thomas Parr Jr., Ph.D.		Form S-1/A (Exhibit 10.7)	10/23/2017	333-220858
10.10#	Employment Agreement, dated October 20, 2017, by and between the Registrant and Cristina Larkin		Form S-1/A (Exhibit 10.8)	10/23/2017	333-220858
10.11#	Employment Agreement, dated December 13, 2017, by and between the Registrant and David Melnick, M.D.		Form 10-K (Exhibit 10.9)	4/2/2018	001-38266
10.12#	Employment Agreement, dated January 1, 2020, by and between the Registrant and Timothy Keutzer	X			
10.13#	Consulting Agreement, dated April 18, 2019, by and between the Registrant and David P. Southwell	X			
10.14#	Lease Agreement, dated August 24, 2015, by and between the Registrant and U.S. REIF Central Plaza Massachusetts, LLC		Form S-1 (Exhibit 10.11)	10/6/2017	333-220858
10.15	First Amendment to Lease Agreement, dated January 17, 2018, by and between the Registrant and U.S. REIF Central Plaza Massachusetts, LLC		Form 8-K (Exhibit 99.1)	1/23/2018	001-38266
10.16	Second Amendment to Lease Agreement, dated December 16, 2019, by and between the Registrant and U.S. REIF Central Plaza Massachusetts, LLC		Form 8-K (Exhibit 99.1)	12/19/2019	001-38266
10.17	Sublease, dated July 6, 2016, by and between the Registrant and Tetraphase Pharmaceuticals, Inc.		Form S-1 (Exhibit 10.12)	10/6/2017	333-220858
10.18†	Stock Purchase Agreement, dated June 6, 2016, by and among Spero Cantab, Inc., the Registrant, Spero Cantab UK Limited, PBB Distributions Limited, New Pharma License Holdings Limited, Cantab Anti-Infectives Ltd and Pro Bono Bio PLC, as amended by Amendment to Stock Purchase Agreement, dated July 18, 2017		Form S-1 (Exhibit 10.13)	10/6/2017	333-220858
10.19†	Assignment and License Agreement, dated May 9, 2016, by and among Spero Trinem, Inc., the Registrant and Vertex Pharmaceuticals Incorporated		Form S-1/A (Exhibit 10.14)	10/23/2017	333-220858
10.20†	License Agreement, dated June 14, 2017, by and between the Registrant and Meiji Seika Pharma Co., Ltd., as supplemented by Addendum to License Agreement, dated June 14, 2017		Form S-1 (Exhibit 10.15)	10/6/2017	333-220858
10.21†	Contract Award, dated July 12, 2018, issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services		Form 10-Q (Exhibit 10.1)	11/8/2018	001-38266
10.22*	License Agreement, dated January 4, 2019, by and between New Pharma License Holdings Limited and Everest Medicines II Limited		Form 10-K (Exhibit 10.20)	3/14/2019	001-38266
10.23	Exchange Agreement, dated November 15, 2018, by and among Spero Therapeutics, Inc. and Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., Biotechnology Value Trading Fund OS, L.P. and MSI BVF SPV LLC		Form 8-K (Exhibit 10.1)	11/16/2018	001-38266

10.24	Controlled Equity Offering Sales Agreement, dated December 3, 2018, by and between the Registrant and Cantor Fitzgerald & Co.		Form S-3 (Exhibit 1.2)	12/3/2018	333-228661
10.25	Securities Purchase Agreement, dated June 12, 2019, by and between the Registrant and Novo Holdings A/S		Form 10-Q (Exhibit 10.1)	8/8/2019	001-38266
10.26	Form of Proprietary Information and Inventions Assignment Agreement		Form S-1/A (Exhibit 10.17)	10/23/2017	333-220858
16.1	Letter of KPMG LLP, dated August 25, 2017, regarding changes in the Registrant's certifying accountants		Form S-1 (Exhibit 16.1)	10/6/2017	333-220858
21.1	List of Subsidiaries of the Registrant	X			
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm	X			
31.1	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X			
31.2	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X			
32.1	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X			
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X			
101.INS	XBRL Instance Document	X			
101.SCH	XBRL Taxonomy Extension Schema Document	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	XBRL Taxonomy Extension Definition	X			
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	XBRL Taxonomy Presentation Linkbase Document	X			

† Confidential treatment received as to portions of the exhibit. Confidential materials omitted and filed separately with the SEC.

Management contract or compensatory plan.

* Confidential treatment requested for portions of this exhibit. Confidential materials omitted and filed separately with the SEC.

Item 16. Form 10-K Summary.

None.

SIGNATURES

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

SPERO THERAPEUTICS, INC.

Date: March 16, 2020

By: /s/ Ankit Mahadevia, M.D.
Ankit Mahadevia, M.D.
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints each of Ankit Mahadevia, M.D. and Stephen J. DiPalma his true and lawful attorney-in-fact and agent, with full power of substitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments to this Annual 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 attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

IN WITNESS WHEREOF, each of the undersigned has executed this Power of Attorney as of the date indicated opposite his name.

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 in the capacities and on the dates indicated.

Name	Title	Date
/s/ Ankit Mahadevia, M.D. Ankit Mahadevia, M.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 16, 2020
/s/ Stephen J. DiPalma Stephen J. DiPalma	Interim Chief Financial Officer and Treasurer *(Principal Financial Officer and Principal Accounting Officer)*	March 16, 2020
/s/ Milind Deshpande, Ph.D. Milind Deshpande, Ph.D.	Director	March 16, 2020
/s/ Jean-François Formela, M.D. Jean-François Formela, M.D.	Director	March 16, 2020
/s/ John C. Pottage, M.D. John C. Pottage, M.D.	Director	March 16, 2020
/s/ Cynthia Smith Cynthia Smith	Director	March 16, 2020
/s/ Frank E. Thomas Frank E. Thomas	Director	March 16, 2020
/s/ Patrick Vink, M.D. Patrick Vink, M.D.	Director	March 16, 2020

Exhibit 4.3

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

Spero Therapeutics, Inc. ("Spero" or the "Company") has one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act").

DESCRIPTION OF COMMON STOCK

We are authorized to issue 60,000,000 shares of common stock, par value $0.001 per share. As of December 31, 2019, we had 19,190,695 shares of common stock outstanding.

The following description of our common stock is a summary and does not purport to be complete. You should refer to our amended and restated certificate of incorporation and our amended and restated bylaws, both of which are incorporated by reference as exhibits to the Company's Annual Report on Form 10-K of which this exhibit is a part. The summary below is also qualified by provisions of applicable law.

General

We are authorized to issue one class of common stock. Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that are currently designated and issued or that we may designate and issue in the future. Except as described under "Certain Provisions of Delaware Law and of the Company's Certificate of Incorporation and Bylaws—Anti-Takeover Provisions" below, a majority vote of the holders of common stock is generally required to take action under our amended and restated certificate of incorporation and amended and restated bylaws.

Transfer Agent and Registrar

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

Stock Exchange Listing

Our common stock is listed for quotation on The Nasdaq Global Select Market under the symbol "SPRO."

CERTAIN PROVISIONS OF DELAWARE LAW AND OF THE COMPANY'S CERTIFICATE OF INCORPORATION AND BYLAWS

Anti-Takeover Provisions

Delaware Law

We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Charter Documents

In accordance with our amended and restated certificate of incorporation, our board is divided into three classes serving three-year terms, with one class being elected each year. The provision for a classified board could prevent a party who acquires control of a majority of our outstanding voting stock from obtaining control of the our board of directors until the second annual stockholders meeting following the date the acquirer obtains the controlling stock interest. Our classified board provision could also discourage a potential acquirer from making a tender offer or otherwise attempting to obtain control of Spero and could increase the likelihood that incumbent directors will retain their positions.

Our amended and restated certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office, even if less than a quorum.

As required by the Delaware General Corporation Law, any amendment of our amended and restated certificate of incorporation must first be approved by a majority of our board of directors and, if required by law or our amended and restated certificate of incorporation, thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability, exclusive jurisdiction of Delaware Courts and the amendment of our amended and restated bylaws and amended and restated certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our amended and restated bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in our amended and restated bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class. These provisions could discourage a potential acquirer from making a tender offer or otherwise attempting to obtain control of Spero and could delay changes in management.

Our amended and restated bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in our amended and restated bylaws. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer’s own slate of directors or otherwise attempting to obtain control of our company.

Our amended and restated bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our amended and restated bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting. The restriction on the ability of our stockholders to call a special meeting means that a proposal to replace one or more directors on our board of directors also could be delayed until the next annual meeting.

Our amended and restated certificate of incorporation also provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. Without the availability of stockholder action by written consent, a holder controlling a majority of our capital stock would not be able to amend Spero’s amended and restated bylaws or remove directors without holding a stockholders’ meeting.

SPERO THERAPEUTICS, INC.

NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

(Last amended December 13, 2019)

The Board of Directors of Spero Therapeutics, Inc. (the "Company") has approved the following Non-Employee Director Compensation Policy (this "Policy"), which establishes compensation to be paid to non-employee directors of the Company, effective upon the completion of the Company's initial public offering ("Effective Time"), to provide an inducement to obtain and retain the services of qualified persons to serve as members of the Company's Board of Directors.

Applicable Persons

This Policy shall apply to each director of the Company who is not an employee of the Company or any Affiliate (each, a "Non-Employee Director"). "Affiliate" shall mean an entity which is a direct or indirect parent or subsidiary of the Company, as determined pursuant to Section 424 of the Internal Revenue Code of 1986, as amended.

Stock Option Grants

All stock option amounts set forth herein shall be subject to automatic adjustment in the event of any stock split or other recapitalization affecting the Company's common stock.

Annual Stock Option Grants

Annually, each Non-Employee Director shall be granted a non-qualified stock option to purchase 7,500 shares of the Company's common stock, on the date of the first meeting of the Board of Directors held following the Company's annual meeting of stockholders in each year commencing in 2018.

Initial Stock Option Grant For Newly Appointed or Elected Directors

Each new Non-Employee Director after the Effective Date shall be granted a non-qualified stock option to purchase 15,000 shares of the Company's common stock, at the first regularly scheduled meeting of the Board of Directors on or after his or her initial appointment or election to the Board of Directors.

Terms for All Option Grants

Unless otherwise specified by the Board of Directors or the Compensation Committee at the time of grant, all options granted under this Policy shall (i) have an exercise price equal to the fair market value of the Company's common stock as determined in the Company's 2017 Stock Incentive Plan, as amended, or any other applicable equity incentive plan then-maintained by the Company (the "Stock Plan") on the date of grant; (ii) terminate on the tenth anniversary of the date of grant and (iii) contain such other terms and conditions as set forth in the form of option agreement approved by the Board of Directors or the Compensation Committee. Subject to the continued service of each Non-Employee Director and unless otherwise specified by the Board of Directors or the Compensation Committee at the time of grant, each annual stock option grant shall vest on the first anniversary of the date of grant and each initial stock option grant shall vest in equal monthly installments until the third anniversary of the date of grant.

Annual Fees

Each Non-Employee Director serving on the Board of Directors and the Audit Committee, the Compensation Committee, the Nominating and Corporate Governance Committee and/or the Development Committee, as applicable, shall be entitled to the following annual amounts (the "Annual Fees"):

Board of Directors or Committee of Board of Directors	Annual Retainer Amount for Member	Annual Retainer Amount for Chair
Board Member	$35,000	-
Chairman of the Board (additional retainer)	$30,000	-
Lead Director, if any (additional retainer)	$18,750	-
Audit Committee	$7,500	$15,000
Compensation Committee	$5,000	$10,000
Nominating and Governance Committee	$4,000	$7,500
Development Committee	$5,000	$10,000

Payments

Payments payable to Non-Employee Directors shall be paid quarterly in arrears promptly following the end of each fiscal quarter, provided that (i) the amount of such payment shall be prorated for any portion of such quarter that such director was not serving on the Board or a committee and (ii) no fee shall be payable in respect of any period prior to the date such director was elected to the Board or a committee.

Except as otherwise set forth in this Policy, all Annual Fees shall be paid for the period from January 1 through December 31 of each year. Such Annual Fees shall be paid in cash, except to the extent that an election is made pursuant to the following provision: Prior to the beginning of each calendar year, a Non-Employee Director may elect to receive all or a portion of his or her base Annual Fee for service as a member of the Board of Directors (i.e., $35,000) in the form of a non-qualified stock option to purchase the number of shares of the Company's common stock as is equal to the Black-Scholes value of such Annual Fee (or portion thereof), which option will be granted on the first business day of the calendar year. Any election made with respect to less than all of a Non-Employee Director's base Annual Fee must be expressed in a 50% increment, i.e., he or she may elect to receive either 50% or 100% of the base Annual Fee in the form of an option. Such option shall vest in four quarterly installments on the last day of each calendar quarter during the calendar year subject to the continued service of the Non-Employee Director. Such option shall (i) be issued under the Stock Plan, (ii) contain such other terms and conditions as set forth in the form of option agreement approved by the Board of Directors or the Compensation Committee, and (iii) have an exercise price equal to the fair market value of the Company's common stock on the date of grant, as determined in accordance with the Stock Plan. Each Non-Employee Director who is newly elected or appointed to the Board of Directors after the Effective Date may make an election to be paid in the form of an option within 30 days of his or her election or appointment (the "Option Election") and any such option shall be granted on the last business day of the month following his or her Option Election for the prorated portion of the cash for the initial calendar year and otherwise in accordance with this paragraph. If no election has been made prior to the first day of the calendar year, then the Non-Employee Director shall receive his or her Annual Fees in the form in which they were paid during the prior calendar year.

Expenses

Upon presentation of documentation of such expenses reasonably satisfactory to the Company, each Non-Employee Director shall be reimbursed for his or her reasonable out-of-pocket business expenses incurred in connection with attending meetings of the Board of Directors and committees thereof or in connection with other business related to the Board of Directors.

Amendments

The Compensation Committee shall periodically review this Policy to assess whether any amendments in the type and amount of compensation provided herein should be made and shall make recommendations to the Board of Directors for its approval of any amendments to this Policy.

Exhibit 10.12

EXECUTIVE EMPLOYMENT AGREEMENT

This Executive Employment Agreement (this "Agreement") is made and entered into as of this 1st day of January, 2020 (the "Effective Date") by and between Spero Therapeutics, Inc., a Delaware corporation ("Company"), and Timothy Keutzer ("Executive").

WHEREAS, Executive is currently employed by Company as its Chief Development Officer, pursuant to the terms of that certain offer letter dated August 3rd 2015 (the "Offer Letter");

WHEREAS, Executive and Company desire to enter into a formal employment agreement to assure the harmonious performance of the affairs of Company and which sets forth the current terms of Executive's employment by Company as well as to enter into a Proprietary Information and Inventions Assignment Agreement (the "Restrictive Covenant Agreement").

WHEREAS, Executive and Company are parties to an Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement dated as of June 24th 2018.

NOW, THEREFORE, in consideration of the mutual promises, terms, provisions, and conditions contained herein, Company and Executive hereby agree to amend and replace the Offer Letter as follows:

1. Roles and Duties. Subject to the terms and conditions of this Agreement, Company shall employ Executive as its Chief Development Officer reporting to Company's Chief Executive Officer ("CEO"). The Executive shall have such duties and responsibilities as are reasonably determined by the Board of Directors and are consistent with the duties customarily performed by a Chief Development Officer of a similarly situated company in the United States. Executive accepts such employment upon the terms and conditions set forth herein, and agrees to perform such duties and discharge such responsibilities to the best of Executive's ability. During Executive's employment, Executive shall devote all of Executive's business time and energies to the business and affairs of Company. Notwithstanding the foregoing, nothing herein shall preclude Executive from (i) performing services for such other companies as Company may designate or permit; (ii) serving, with the prior written consent of the Board, which consent shall not be unreasonably withheld, as a member of the boards of directors or advisory boards (or their equivalents in the case of a non-corporate entity) of non-competing businesses or charitable, educational or civic organizations; (iii) engaging in charitable activities and community affairs; and (iv) managing Executive's personal investments and affairs; provided, however, that the activities set out in clauses (i), (ii), (iii) and (iv) shall be limited by Executive so as not to materially interfere, individually or in the aggregate, with the performance of Executive's duties and responsibilities hereunder.

2. Term of Employment.

(a) Term. Subject to the terms hereof, Executive's employment hereunder shall continue until terminated hereunder by either party (such term of employment referred to herein as the "Term").

(b) Termination. Notwithstanding anything else contained in this Agreement, Executive's employment hereunder shall terminate upon the earliest to occur of the following:

(i) Death. Immediately upon Executive's death;

(ii) Termination by Company.

(A) If because of Executive's Disability (as defined below in Section 2(c)), written notice by Company to Executive that Executive's employment is being terminated as a result of Executive's Disability, which termination shall be effective on the date of such notice or such later date as specified in writing by Company;

(B) If for Cause (as defined below in Section 2(d)), written notice by Company to Executive that Executive's employment is being terminated for Cause, which termination shall be effective on the date of such notice or such later date as specified in writing by Company, provided that if prior to the effective date of such termination Executive has cured the circumstances giving rise to the Cause (if capable of being cured as provided in Section 2(d)), then such termination shall not be effective; or

(C) If by Company for reasons other than under Sections 2(b)(ii)(A) or (B), written notice by Company to Executive that Executive's employment is being terminated, which termination shall be effective thirty (30) days after the date of such notice.

(iii) Termination by Executive.

(A) If for Good Reason (as defined below in Section 2(e)), written notice by Executive to Company that Executive is terminating Executive's employment for Good Reason and that sets forth the factual basis supporting the alleged Good Reason, which termination shall be effective thirty (30) days after the date of such notice; provided that if prior to the effective date of such termination Company has cured the circumstances giving rise to the Good Reason if capable of being cured as provided in Section 2(e), then such termination shall not be effective; or

(B) If without Good Reason, written notice by Executive to Company that Executive is terminating Executive's employment, which termination shall be effective no fewer than sixty (60) days after the date of such notice unless waived, in whole or in part, by Company.

Notwithstanding anything in this Section 2(b), Company may at any point, under the conditions set forth in Section 2(b)(ii)(B), terminate Executive's employment for Cause prior to the effective date of any other termination contemplated hereunder; provided that if prior to the effective date of such for-Cause termination Executive has cured the circumstances giving rise to the Cause (if capable of being cured as provided in Section 2(d)), then such termination shall not be effective.

(c) Definition of "Disability". For purposes of this Agreement, "Disability" shall mean Executive's incapacity or inability to perform Executive's duties and responsibilities as contemplated herein by reason of a medically determinable mental or physical impairment for one hundred twenty (120) days or more within any one (1) year period (cumulative or consecutive), which impairment can reasonably be expected to result in death or can be expected to last for a continuous period of not less than six (6) months. The determination that Executive is disabled hereunder, if disputed by the parties, shall be resolved by a physician reasonably satisfactory to Executive and Company, at Company's expense, and the determination of such physician shall be final and binding upon both Executive and Company. Executive hereby consents to such examination and consultation by a physician. Company will keep all information it receives as a result of such inquiry and determination confidential and will not use it for any purpose other than in connection with exercising its rights under this Agreement.

(d) Definition of "Cause". As used herein, "Cause" shall mean: (i) Executive's conviction of (A) a felony or (B) any misdemeanor involving moral turpitude, deceit, dishonesty or fraud; (ii) Executive's willful failure or refusal to comply with lawful directions of the CEO, which failure or refusal continues for more than thirty (30) days after written notice is given to Executive by the CEO, which notice sets forth in reasonable detail the nature of such failure or refusal; (iii) willful and material breach by Executive of a written Company policy applicable to Executive or Executive's covenants and/or obligations under this Agreement or the material breach of the Restrictive Covenant Agreement; and/or (iv) material misconduct by Executive that seriously discredits or damages Company or any of its affiliates. Except in the case of (ii) above, it is not necessary that the Company's finding of Cause occur prior to Executive's termination of service. If Company determines, subsequent to Executive's termination of service, that prior to Executive's termination Executive engaged in conduct which would constitute "Cause," (other than pursuant to (ii) above) then Executive shall have no right to any benefit or compensation under this Agreement.

(e) Definition of "Good Reason". As used herein, "Good Reason" shall mean: (i) relocation of Executive's principal business location to a location more than thirty (30) miles from Executive's then-current business location; (ii) a material diminution in Executive's duties, authority or responsibilities; (iii) a material reduction in Executive's Base Salary; or (iv) willful and material breach by Company of its covenants and/or obligations under this Agreement; provided that, in each of the foregoing clauses (i) through (iv) (A) Executive provides Company with written notice that Executive intends to terminate Executive's employment hereunder for one of the grounds set forth in this Section 2(e) within thirty (30) days of such ground occurring, (B) if such ground is capable of being cured, Company has failed to cure such ground within a period of thirty (30) days from the date of such written notice, and (C) Executive terminates by written notice Executive's employment within sixty-five (65) days from the date that Executive provides the notice contemplated by clause (A) of this Section 2(e). For purposes of clarification, the above-listed conditions shall apply separately to each occurrence of Good Reason, and failure to adhere

to such conditions in the event of Good Reason shall not disqualify Executive from asserting Good Reason for any subsequent occurrence of Good Reason. In addition, Executive may terminate his employment for Good Reason within one (1) year following a Change of Control (as defined below) if, after the Change of Control, Executive is not an executive of the parent company, provided that Executive's roles, responsibilities and scope of authority within the subsidiary is not comparable to Executive's roles, responsibilities and scope of authority with Company prior to the Change of Control. For purposes of this Agreement, "Good Reason" shall be interpreted in a manner, and limited to the extent necessary, so that it shall not cause adverse tax consequences for either party with respect to Section 409A ("Section 409A") of the Internal Revenue Code of 1986, as amended (the "Code") and any successor statute, regulation and guidance thereto.

3. Compensation.

(a) Base Salary. Company shall pay Executive a base salary (the "Base Salary") at the annual rate of Three Hundred Thirty Thousand Dollars ($330,000). The Base Salary shall be payable in substantially equal periodic installments in accordance with Company's payroll practices as in effect from time to time. Company shall deduct from each such installment all amounts required to be deducted or withheld under applicable law or under any employee benefit plan in which Executive participates. The Board or an appropriate committee thereof shall, on an annual basis, review the Base Salary, which may be adjusted upward (but not downward) at Company's discretion.

(b) Annual Performance Bonus. Executive shall be eligible to receive an annual cash bonus (the "Annual Performance Bonus"), with the target amount of such Annual Performance Bonus equal to forty percent (40%) of Executive's Base Salary in the year to which the Annual Performance Bonus relates; provided that the actual amount of the Annual Performance Bonus may be greater or less than such target amount. The amount of the Annual Performance Bonus shall be determined by the Board of Directors or an appropriate committee thereof in its sole discretion, and shall be paid to Executive no later than March 15th of the calendar year immediately following the calendar year in which it was earned. Except as provided in Section 4, Executive must be employed by Company on the last day of the applicable fiscal year to which the Annual Performance Bonus relates in order to be eligible for, and to be deemed as having earned, such Annual Performance Bonus. Company shall deduct from the Annual Performance Bonus all amounts required to be deducted or withheld under applicable law or under any employee benefit plan in which Executive participates.

(c) Equity. In addition to the equity awards currently outstanding, Executive will be eligible to be considered for the grant of stock options and/or other equity-based awards commensurate with Executive's position and responsibilities. The amount, terms and conditions of any stock option or other equity-based award will be determined by the Board of Directors or an appropriate committee thereof in its discretion and set forth in the applicable equity plan and other documents governing the award.

(d) Paid Time Off. In addition to standard paid holidays, Executive may take up to twenty (20) days of paid time off ("PTO") per year, to be scheduled so as not to materially disrupt Company's operations, pursuant to the terms and conditions of Company policy and practices as applied to Company senior executives.

(e) Fringe Benefits. Executive shall be entitled to participate in all benefit/welfare plans and fringe benefits provided to Company senior executives. Executive understands that, except when prohibited by applicable law, Company's benefit plans and fringe benefits may be amended by Company from time to time in its sole discretion. The terms of any such benefits shall be governed by the applicable plan documents and Company policies in effect from time to time.

(f) Reimbursement of Expenses. Company shall reimburse Executive for all ordinary and reasonable out-of-pocket business expenses incurred by Executive in furtherance of Company's business in accordance with Company's policies with respect thereto as in effect from time to time. Executive must submit any request for reimbursement no later than ninety (90) days following the date that such business expense is incurred. All reimbursements provided under this Agreement shall be made or provided in accordance with the requirements of Section 409A including, where applicable, the requirement that (i) any reimbursement is for expenses incurred during Executive's lifetime (or during a shorter period of time specified in this Agreement); (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year; (iii) the reimbursement of an eligible expense shall be made no later than the last day of the calendar year following the year in which the expense is incurred; and (iv) the right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

(g) Indemnification. Executive shall be entitled to indemnification with respect to Executive's services provided hereunder pursuant to Delaware law, the terms and conditions of Company's certificate of incorporation and/or by-laws, and Company's standard indemnification agreement for directors and officers as executed by Company and Executive. Executive shall be entitled to coverage under the Company's Directors' and Officers' ("D&O") insurance policies that it may hold now or in the future to the same extent and in the same manner (i.e., subject to the same terms and conditions) that the Company's other executive officers are entitled to coverage under any of the Company's D&O insurance policies that it may have.

(h) Forfeiture/Clawback. All compensation shall be subject to any forfeiture or clawback policy established by Company generally for senior executives from time to time and any other such policy required by applicable law.

4. Payments Upon Termination.

(a) Definition of Accrued Obligations. For purposes of this Agreement, "Accrued Obligations" means: (i) the portion of Executive's Base Salary that has accrued prior to any termination of Executive's employment with Company and has not yet been paid; (ii) any accrued but unused PTO pursuant to Company's standard policy and practices; and (iii) the amount of any expenses properly incurred by Executive on behalf of Company prior to any such termination and not yet reimbursed. Executive's entitlement to any other compensation or benefit under any plan of Company shall be governed by and determined in accordance with the terms of such plans, except as otherwise specified in this Agreement.

(b) Termination by Company for Cause. If Executive's employment hereunder is terminated by Company for Cause, then Company shall pay the Accrued Obligations to Executive promptly following the effective date of such termination and shall have no further obligations with respect to any benefit or compensation under this Agreement to Executive hereunder.

(c) Termination by Executive Without Good Reason. If Executive's employment hereunder is terminated by Executive without Good Reason, then Company shall pay the Accrued Obligations and any accrued and unpaid Annual Performance Bonus for the prior fiscal year to Executive promptly following the effective date of such termination and shall have no further obligations with respect to any benefit or compensation under this Agreement to Executive hereunder.

(d) Termination as a Result of Executive's Disability or Death. If Executive's employment hereunder terminates as a result of Executive's Disability or death, promptly after such termination Company shall pay to Executive (i) the Accrued Obligations; (ii) any accrued and unpaid Annual Performance Bonus for the prior fiscal year; and (iii) the Pro Rated Bonus (as defined below) and, shall have no further obligations with respect to any benefit or compensation under this Agreement to Executive hereunder. As used in this Section 4, "Pro Rated Bonus" shall mean an amount in cash equal to the target of Annual Performance Bonus for which Executive would have been eligible with respect to the year in which termination of Executive's employment occurs multiplied by a fraction, the numerator of which is the number of days during which Executive is employed by Company during the year of termination and the denominator of which is 365.

(e) Termination by Company Without Cause or by Executive For Good Reason. In the event that Executive's employment is terminated by action of Company other than for Cause, or Executive terminates Executive's employment for Good Reason, then, in addition to the Accrued Obligations and any accrued and unpaid Annual Performance Bonus for the prior fiscal year, Executive shall receive the following, subject to the terms and conditions described in Section 4(g) (including Executive's execution of the Release (as defined herein)):

(i) Severance Payments. Continuation of payments in an amount equal to Executive's then-current Base Salary for a nine (9) month period, less all customary and required taxes and employment-related deductions, in accordance with Company's normal payroll practices (provided such payments shall be made at least monthly), commencing on the first payroll date following the date on which the Release required by Section 4(g) becomes effective and non-revocable, but not after seventy (70) days following the effective date of termination from employment; provided, that if the 70th day falls in the calendar year following the year during which the termination or separation from service occurred, then the payments will commence in such subsequent calendar year; provided further that if such payments commence in such subsequent year, the first such payment shall be a lump sum in an amount equal to the payments that would have come due since Employee's separation from service.

(ii) Pro Rata Bonus. Payment of the Pro Rated Bonus, paid to Executive no later than March 15 of the calendar year next preceding the year of termination of employment, after deduction of all amounts required to be deducted or withheld under applicable law.

(iii) Benefits Payments. Upon completion of appropriate forms and subject to applicable terms and conditions under the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended ("COBRA"), Company shall continue to provide Executive medical insurance coverage to the same extent that such insurance continues to be provided to similarly situated executives at the time of Executive's termination with the cost of the regular premium for such benefits shared in the same relative proportion by Company and Executive as in effect on the last day of employment (the "COBRA Payment"), until the earlier to occur of: (i) twelve (12) months following Executive's termination date, or (ii) the date Executive becomes eligible for medical benefits with another employer. Notwithstanding the foregoing, if Executive's COBRA Payment would cause the applicable group health plan to be discriminatory and, therefore, result in adverse tax consequences to Executive, Company shall, in lieu of the COBRA Payment, provide Executive with an equivalent monthly cash payment, minus deduction of all amounts required to be deducted or withheld under applicable law, for any period of time Executive is eligible to receive the COBRA Payment. Executive shall bear full responsibility for applying for COBRA continuation coverage and Company shall have no obligation to provide Executive such coverage if Executive fails to elect COBRA benefits in a timely fashion.

Payment of the above described severance payments and benefits are expressly conditioned on Executive's execution without revocation of the Release and return of Company property under Section 6.

(f) Termination by Company Without Cause or by Executive For Good Reason Following a Change of Control. In the event that a Change of Control (as defined below) occurs and within a period of one (1) year following the Change of Control, or ninety (90) days preceding the earlier to occur of a Change of Control or the execution of a definitive agreement the consummation of which would result in a Change of Control, Executive's employment is terminated other than for Cause, or Executive terminates Executive's employment for Good Reason, then, in addition to the Accrued Obligations and any accrued and unpaid Annual Performance Bonus for the prior fiscal year, Executive shall receive the following, subject to the terms and conditions described in Section 4(g) (including Executive's execution of the Release):

(i) Lump Sum Severance Payment. Payment of a lump sum amount equal to twelve (12) months of Executive's then-current Base Salary plus the Pro Rated Bonus, less all customary and required taxes and employment-related deductions, paid on the first payroll date following the date on which the Release required by Paragraph 4(g) becomes effective and non-revocable, but not after seventy (70) days following the effective date of termination from employment.

(ii) Equity Acceleration. On the date of termination of Executive's employment, Executive shall become fully vested in any and all equity awards outstanding as of the date of Executive's termination and this provision shall supersede any option acceleration provision contained in any option agreement outstanding on the Effective Date.

(iii) Benefit Payments. Upon completion of appropriate forms and subject to applicable terms and conditions under COBRA, Company shall continue to provide Executive medical insurance coverage to the same extent that such insurance continues to be provided to similarly situated executives at the time of Executive's termination with the cost of the regular premium for such benefits shared in the same relative proportion by Company and Executive as in effect on the last day of employment, until the earlier to occur of: (i) twelve (12) months following Executive's termination date, or (ii) the date Executive becomes eligible for medical benefits with another employer. Notwithstanding the foregoing, if Executive's COBRA Payment would cause the applicable group health plan to be discriminatory and, therefore, result in adverse tax consequences to Executive, Company shall, in lieu of the COBRA Payment, provide Executive with an equivalent monthly cash payment, minus deduction of all amounts required to be deducted or withheld under applicable law, for any period of time Executive is eligible to receive the COBRA Payment. Executive shall bear full responsibility for applying for COBRA continuation coverage and Company shall have no obligation to provide Executive such coverage if Executive fails to elect COBRA benefits in a timely fashion.

Payment of the above described severance payments and benefits are expressly conditioned on Executive's execution without revocation of the Release and return of Company property under Section 6. In the event that Executive is eligible for the severance payments and benefits under this Section 4(f), Executive shall not be eligible for any of the severance payments and benefits as provided in Section 4(e).

As used herein, a "Change of Control" shall mean the occurrence of any of the following events: (i) Ownership. Any "Person" (as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended) becomes the "Beneficial Owner" (as defined in Rule 13d-3 under said Act), directly or indirectly, of securities of Company representing fifty percent (50%) or more of the total voting power represented by Company's then outstanding voting securities (excluding for this purpose any such voting securities held by Company, or any affiliate, parent or subsidiary of Company, or by any employee benefit plan of Company) pursuant to a transaction or a series of related transactions; or (ii) Merger/Sale of Assets. (A) A merger or consolidation of Company whether or not approved by the Board, other than a merger or consolidation which would result in the voting securities of Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or the parent of such corporation) at least fifty percent (50%) of the total voting power represented by the voting securities of Company or such surviving entity or parent of such corporation, as the case may be, outstanding immediately after such merger or consolidation; (B) or Company's stockholders approve an agreement for the sale or disposition by Company of all or substantially all of Company's assets; or (iii) Change in Board Composition. A change in the composition of the Board, as a result of which fewer than a majority of the directors

are Incumbent Directors. “Incumbent Directors” shall mean directors who either (A) are directors of Company as of the date of this Agreement, or (B) are elected, or nominated for election, to the Board with the affirmative votes of at least a majority of the Incumbent Directors, or by a committee of the Board made up of at least a majority of the Incumbent Directors, at the time of such election or nomination (but shall not include an individual whose election or nomination is in connection with an actual or threatened proxy contest relating to the election of directors).

(g) Execution of Release of Claims. Company shall not be obligated to pay Executive any of the severance payments or benefits described in this Section 4 unless and until Executive has executed (without revocation) a release of claims as described below (the “Release”). The Release shall contain reasonable and customary provisions including a general release of claims against Company and its affiliated entities and each of their officers, directors and employees as well as mutual non-disparagement, confidentiality, cooperation and the like. The Release must be provided to Executive not later than fifteen (15) days following the effective date of termination of Executive’s employment by Company and executed by Executive and returned to Company within sixty (60) days after such effective date. If Executive fails or refuses to return the Release within such 60-day period, Executive’s severance payments and benefits to be paid hereunder shall be forfeited.

(h) No Other Payments or Benefits Owing. Except as expressly set forth herein, the payments and benefits set forth in this Section 4: (a) shall be the sole amounts owing to Executive upon termination of Executive’s employment for the reasons set forth above, and Executive shall not be eligible for any other payments or other forms of compensation or benefits; (b) shall be the sole remedy, if any, available to Executive in the event that Executive brings any claim against Company relating to the termination of Executive’s employment under this Agreement; and (c) shall not be subject to set-off by Company or any obligation on the part of Executive to mitigate or to offset compensation earned by Executive in other pursuits after termination of employment, other than as specified herein with respect medical benefits provided by another employer.

5. Prohibited Competition and Solicitation. Executive expressly acknowledges that: (a) there are competitive and proprietary aspects of the business of Company; (b) during the course of Executive’s employment, Company shall furnish, disclose or make available to Executive confidential and proprietary information and may provide Executive with unique and specialized training; (c) such Confidential Information and training have been developed and shall be developed by Company through the expenditure of substantial time, effort and money, and could be used by Executive to compete with Company; and (d) in the course of Executive’s employment, Executive shall be introduced to customers and others with important relationships to Company, and any and all “goodwill” created through such introductions belongs exclusively to Company, including, but not limited to, any goodwill created as a result of direct or indirect contacts or relationships between Executive and any customers of Company.

6. Property and Records. Upon the termination of Executive's employment hereunder for any reason or for no reason, or if Company otherwise requests, Executive shall: (a) return to Company all tangible business information and copies thereof (regardless how such Confidential Information or copies are maintained), and (b) deliver to Company any property of Company which may be in Executive's possession, including, but not limited to, Blackberry-type devices, smart phones, laptops, cell phones (the foregoing, "electronic devices"), products, materials, memoranda, notes, records, reports or other documents or photocopies of the same. Executive may retain copies of any exclusively personal data contained in or on Company-owned electronic devices returned to Company pursuant to the foregoing. The foregoing notwithstanding, Executive understands and agrees that Company property belongs exclusively to Company, it should be used for Company business, and Executive has no reasonable expectation of privacy on any Company property or with respect to any information stored thereon.

7. Cooperation. During and after Executive's employment, Executive shall fully cooperate with Company to the extent reasonable in the defense or prosecution of any claims or actions now in existence or which may be brought in the future against or on behalf of Company (other than claims directly or indirectly against Executive) which relate to events or occurrences that transpired while Executive was employed by Company. Executive's cooperation in connection with such claims or actions shall include, but not be limited to, being available to meet with counsel to prepare for discovery or trial and to act as a witness on behalf of Company at mutually convenient times. During and after Executive's employment, Executive also shall fully cooperate with Company to the extent reasonable in connection with any investigation or review of any federal, state or local regulatory authority as any such investigation or review relates to events or occurrences that transpired while Executive was employed by Company. Company shall reimburse Executive for any reasonable out-of-pocket expenses incurred in connection with the Executive's performance of obligations pursuant to this section. In addition, Company shall compensate Executive on an hourly basis, based on a rate commensurate with Executive's Base Salary in effect prior to termination, for time Executive spends in excess of 10 hours in any calendar quarter providing services to the Corporation after termination.

8. Code Sections 409A and 280G.

(a) In the event that the payments or benefits set forth in Section 4 of this Agreement constitute "non-qualified deferred compensation" subject to Section 409A, then the following conditions apply to such payments or benefits:

(i) Any termination of Executive's employment triggering payment of benefits under Section 4 must constitute a "separation from service" under Section 409A(a)(2)(A)(i) of the Code and Treas. Reg. §1.409A-1(h) before distribution of such benefits can commence. To the extent that the termination of Executive's employment does not constitute a separation of service under Section 409A(a)(2)(A)(i) of the Code and Treas. Reg. §1.409A-1(h) (as the result of further services that are reasonably anticipated to be provided by Executive to Company at the time Executive's employment terminates), any such payments under Section 4 that constitute deferred compensation under Section 409A shall be delayed until after the date of a subsequent event constituting a separation of service under Section 409A(a)(2)(A)(i) of the Code and Treas. Reg. §1.409A-1(h). For purposes of clarification, this Section 8(a) shall not cause any forfeiture of benefits on Executive's part, but shall only act as a delay until such time as a "separation from service" occurs.

(ii) Notwithstanding any other provision with respect to the timing of payments under Section 4 if, at the time of Executive's termination, Executive is deemed to be a "specified employee" of Company (within the meaning of Section 409A(a)(2)(B)(i) of the Code), then limited only to the extent necessary to comply with the requirements of Section 409A, any payments to which Executive may become entitled under Section 4 which are subject to Section 409A (and not otherwise exempt from its application) shall be withheld until the first (1st) business day of the seventh (7th) month following the termination of Executive's employment, at which time Executive shall be paid an aggregate amount equal to the accumulated, but unpaid, payments otherwise due to Executive under the terms of Section 4.

(b) It is intended that each installment of the payments and benefits provided under Section 4 of this Agreement shall be treated as a separate "payment" for purposes of Section 409A. Neither Company nor Executive shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

(c) Notwithstanding any other provision of this Agreement to the contrary, this Agreement shall be interpreted and at all times administered in a manner that avoids the inclusion of compensation in income under Section 409A, or the payment of increased taxes, excise taxes or other penalties under Section 409A. The parties intend this Agreement to be in compliance with Section 409A. Executive acknowledges and agrees that Company does not guarantee the tax treatment or tax consequences associated with any payment or benefit arising under this Agreement, including but not limited to consequences related to Section 409A.

(d) If any payment or benefit Executive would receive under this Agreement, when combined with any other payment or benefit Executive receives pursuant to a Change of Control (for purposes of this section, a "Payment") would: (i) constitute a "parachute payment" within the meaning of Section 280G the Code; and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either: (A) the full amount of such Payment; or (B) such lesser amount (with cash payments being reduced before stock option compensation) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employments taxes, income taxes, and the Excise Tax, results in Executive's receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax. Notwithstanding the foregoing, if, prior to the closing of an initial public offering, any Payment can be exempt from the definition of "parachute payment" and the Excise Tax pursuant to the shareholder approval requirements described in Treas. Regs. § 1.280G-1, Q&A 6, the Company will, at the Executive's election (and subject to the Executive signing an appropriate waiver) seek shareholder approval to exempt such Payment from the definition of "parachute payment" and the Excise Tax.

9. General.

(a) Notices. Except as otherwise specifically provided herein, any notice required or permitted by this Agreement shall be in writing and shall be delivered as follows with notice deemed given as indicated: (i) by personal delivery when delivered personally; (ii) by overnight courier upon written verification of receipt; (iii) by telecopy or facsimile transmission upon acknowledgment of receipt of electronic transmission; or (iv) by certified or registered mail, return receipt requested, upon verification of receipt.

Notices to Executive shall be sent to the last known address in Company's records or such other address as Executive may specify in writing.

Notices to Company shall be sent to:

Spero Therapeutics, Inc.
675 Massachusetts Ave., 14th Floor
Cambridge, MA 02139
Attn: CEO

(b) Modifications and Amendments. The terms and provisions of this Agreement may be modified or amended only by written agreement executed by the parties hereto.

(c) Waivers and Consents. The terms and provisions of this Agreement may be waived, or consent for the departure therefrom granted, only by a written document executed by the party entitled to the benefits of such terms or provisions. No such waiver or consent shall be deemed to be or shall constitute a waiver or consent with respect to any other terms or provisions of this Agreement, whether or not similar. Each such waiver or consent shall be effective only in the specific instance and for the purpose for which it was given and shall not constitute a continuing waiver or consent.

(d) Assignment. Company may assign its rights and obligations hereunder to any person or entity that succeeds to all or substantially all of Company's business or that aspect of Company's business in which Executive is principally involved. Executive may not assign Executive's rights and obligations under this Agreement without the prior written consent of Company.

(e) Governing Law/Dispute Resolution. This Agreement and the rights and obligations of the parties hereunder shall be construed in accordance with and governed by the law of the Commonwealth of Massachusetts without giving effect to the conflict of law principles thereof. Any legal action or proceeding with respect to this Agreement shall be brought in the courts of the Commonwealth of Massachusetts or of the United States of America for the District of Massachusetts. By execution and delivery of this Agreement, each of the parties hereto accepts for itself and in respect of its property, generally and unconditionally, the non-exclusive jurisdiction of the aforesaid courts.

(f) Jury Waiver. ANY, ACTION, DEMAND, CLAIM, OR COUNTERCLAIM ARISING UNDER OR RELATING TO THIS AGREEMENT SHALL BE RESOLVED BY A JUDGE ALONE, AND EACH OF COMPANY AND EXECUTIVE WAIVES ANY RIGHT TO A JURY TRIAL THEREOF.

(g) Headings and Captions. The headings and captions of the various subdivisions of this Agreement are for convenience of reference only and shall in no way modify or affect the meaning or construction of any of the terms or provisions hereof.

(h) Entire Agreement. This Agreement, together with the other agreements specifically referenced herein, embodies the entire agreement and understanding between the parties hereto with respect to the subject matter hereof and supersedes all prior oral or written agreements and understandings relating to the subject matter hereof. No statement, representation, warranty, covenant or agreement of any kind not expressly set forth in this Agreement shall affect, or be used to interpret, change or restrict, the express terms and provisions of this Agreement.

(i) Counterparts. This Agreement may be executed in two or more counterparts, and by different parties hereto on separate counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. For all purposes a signature by fax shall be treated as an original.

[Signature Page to Follow]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first written above.

TIMOTHY KEUTZER	**SPERO THERAPEUTICS, INC.**
/s/ Timothy Keutzer	By:/s/ Ankit Mahadevia
Signature	Ankit Mahadevia
Timothy Keutzer	Chief Executive Officer

Address:

Exhibit 10.13

675 Massachusetts Avenue, 14th Floor
Cambridge, MA 02139

April 18, 2019

Mr. David P. Southwell
_____
_____

Dear Mr. Southwell:

This letter agreement sets forth the terms upon which Spero Therapeutics, Inc., a Delaware corporation (the "Company"), agrees to enter into an advisory agreement with you ("Advisor"), effective upon your resignation from the Board of Directors of the Company on the date hereof (the "Effective Date"). The Company and Advisor (each, a "party" and together, the "parties") hereby agree as follows:

1. As of the Effective Date, Advisor shall provide advisory services to the Company (the "Services") on matters relating to the business, strategy and operations of the Company and its subsidiaries, as may be requested by the Company from time to time, but in no event to exceed 60 hours in any given calendar year, prorated for any partial calendar year during the Term (as defined below).
2. The term of this Agreement shall commence as of the Effective Date and continue until April 24, 2020; thereafter, this Agreement shall be automatically extended and will continue in accordance with its terms until terminated by either party upon three (3) days' prior notice by either party to the other (the "Term").
3. In consideration of the Services to be provided, the Company shall pay the Advisor an annual fee of $35,000, payable quarterly, in arrears, promptly following the end of each calendar quarter, prorated for any partial calendar quarter. Additionally, the Company shall reimburse Advisor for Advisor's reasonable business expenses incurred during the Term in connection with Advisor's duties hereunder. Advisor will provide the Company, on a quarterly basis, with summary documentation of his hours worked and verification of any business expenses incurred.

4. Advisor's Services constitute service as a Consultant, as defined under the Company's 2017 Stock Incentive Plan, as amended, and during the Term, Advisor's outstanding stock option to purchase 12,146 shares granted on March 30, 2018 and outstanding stock option to purchase 6,073 shares granted on June 5, 2018 (the "Options") will remain exercisable and continue to vest, pursuant to their terms.

5. The Company has provided and shall provide Advisor with Confidential Information (defined below). Advisor shall not, except as Advisor in good faith deems appropriate to perform Advisor's duties hereunder or as required by applicable law or regulation, governmental investigation, subpoena, or in connection with enforcing the terms of this Agreement (or any agreement referenced herein) without limitation in time, communicate, divulge, disseminate, disclose to others or otherwise use, whether directly or indirectly, any Confidential Information regarding the Company or any of its subsidiaries or affiliates. "Confidential Information" shall mean information about the Company or any of its subsidiaries or affiliates, and their respective businesses, employees, consultants, contractors, clients and customers that is not disclosed by the Company or any of its subsidiaries or affiliates for financial reporting purposes or otherwise generally made available to the public (other than by Advisor's breach of the terms hereof or the terms of any previous confidentiality obligation by Advisor to the Company) and that was learned or developed by Advisor in the course of providing services to the Company or any of its subsidiaries or affiliates, including (without limitation) any proprietary knowledge, trade secrets, data, formulae, information and client and customer lists and all papers, resumes, and records (including computer records) of the documents containing such Confidential Information. Advisor acknowledges that such Confidential Information is specialized, unique in nature and of great value to the Company and its subsidiaries or affiliates, and that such information gives the Company and its subsidiaries or affiliates a competitive advantage.

6. All Advisor Developments are and shall be made for hire by Advisor for the Company or any of its subsidiaries or affiliates. "Advisor Developments" means any discovery, invention, design, method, technique, improvement, enhancement, development, computer program, machine, algorithm or other work or authorship that (i) relates to the business or operations of the Company or any of its subsidiaries or affiliates, or (ii) results from or is suggested by any undertaking assigned to Advisor or work performed by Advisor for or on behalf of the Company or any of its subsidiaries or affiliates, whether created alone or with others, during or after working hours (including before the Effective Date). All Confidential Information and all Advisor Developments shall remain the sole property of the Company or any of its subsidiaries or affiliates. Advisor has not acquired and shall not acquire any proprietary interest in any Confidential Information or Advisor Developments developed or acquired during the Term or during Advisor's service with the Company before the Effective Date. To the extent Advisor may, by operation of law or otherwise, acquire any right, title or interest in or to any Confidential Information or Advisor Development, Advisor hereby assigns to the Company all such proprietary rights. Advisor shall, both during and after the Term, upon the Company's request, promptly execute and deliver to the Company all such assignments, certificates and instruments, and shall promptly perform such other acts, as the Company may from time to time in its discretion deem necessary or desirable to evidence, establish, maintain, perfect, enforce or defend the Company's rights in Confidential Information and Advisor Developments.

7. This letter agreement will be governed by the laws of the Commonwealth of Massachusetts, without regard to conflicts of laws principles. This letter agreement may be executed in counterparts, all of which together shall constitute one and the same agreement. Any signature page delivered by facsimile or electronic image transmission shall be binding to the same extent as an original signature page. This Agreement and the Options constitute the entire agreement between the parties and, as of the Effective Date, terminates and supersedes any and all prior agreements and understandings (whether written or oral) between the parties with respect to the subject matter of this Agreement.

If the foregoing terms are acceptable to you, please indicate your agreement by in the space provided below and returning it to the undersigned at your earliest convenience.

Regards,

/s/ Ankit Mahadevia, M.D.
Ankit Mahadevia, M.D.
Chief Executive Officer

ACKNOWLEDGED & AGREED AS OF APRIL 18, 2019:

/s/ David P. Southwell
David P. Southwell

Exhibit 21.1

SUBSIDIARIES OF SPERO THERAPEUTICS, INC.

Subsidiary	Jurisdiction
New Pharma License Holdings	Malta
Spero Cantab, Inc.	Delaware
Spero Cantab UK Limited	England and Wales
Spero Europe, Ltd.	England and Wales
Spero Legacy STI, Inc.	Delaware
Spero Potentiator, Inc.	Delaware
Spero Potentiator PTY LTD	Australia
Spero Securities Corporation	Massachusetts

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-228661) and Form S-8 (Nos. 333-230283, 333-230281, and 333-222060) of Spero Therapeutics, Inc. of our report dated March 16, 2020 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 16, 2020

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, Ankit Mahadevia, M.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Spero Therapeutics, 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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) 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

   (d) 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 16, 2020

By: /s/ Ankit Mahadevia, M.D.
Ankit Mahadevia, M.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, Stephen J. DiPalma, certify that:

1. I have reviewed this Annual Report on Form 10-K of Spero Therapeutics, 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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) 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

   (d) 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 16, 2020

By: /s/ Stephen J. DiPalma
Stephen J. DiPalma
Interim Chief Financial Officer and Treasurer
(Principal Financial Officer and Principal 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 Spero Therapeutics, Inc. (the "Company") for the period ended December 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(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 result of operations of the Company.

Date: March 16, 2020

By: /s/ Ankit Mahadevia, M.D.
Ankit Mahadevia, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

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 Spero Therapeutics, Inc. (the "Company") for the period ended December 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(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 result of operations of the Company.

Date: March 16, 2020

By: /s/ Stephen J. DiPalma
Stephen J. DiPalma
Interim Chief Financial Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer)