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, 2017

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:

Common Stock, $0.001 par value per share	The Nasdaq Global Select Market
(Title of each class)	**(Name of each exchange on which registered)**

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). YES ☒ NO ☐

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

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

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒ (Do not check if a small reporting company)	Small reporting company	☐
		Emerging growth company	☒

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

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

As of June 30, 2017, the last business day of the registrant's most recently completed second fiscal quarter, there was no established public market for the registrant's common stock. The registrant therefore cannot calculate the aggregate market value of its voting and non-voting common equity held by non-affiliates as of such date. The registrant's common stock began trading on the The Nasdaq Global Select Market on November 2, 2017.

As of March 28, 2018, the registrant had 14,369,182 shares of common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A relating to the 2018 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2017. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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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 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, liquidity and needs for additional financing and our anticipated future cash position;
- our financial performance;
- developments relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under Part II, 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 II 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 novel treatments for multi-drug resistant, or MDR, bacterial infections. Our most advanced product candidate, SPR994, 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. We also have a platform technology known as our Potentiator Platform that we believe will enable us to develop drugs that will expand the spectrum and potency of existing antibiotics, including formerly inactive antibiotics, against Gram-negative bacteria. Our lead product candidates generated from our Potentiator Platform are two intravenous, or IV,-administered agents, SPR741 and SPR206, designed to treat MDR Gram-negative infections in the hospital setting. In addition, we are developing SPR720, an oral antibiotic designed for the treatment of an orphan disease called pulmonary non-tuberculous mycobacterial infections, or NTM. 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 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, highlights 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:

- ***SPR994: Novel Antibiotic with Potential to be the First Broad-Spectrum Oral Carbapenem for Use in Adults***. SPR994 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. While we are developing SPR994 to be effective against a broad spectrum of MDR bacterial infections, our initial focus is on the treatment of complicated urinary tract infections, or cUTIs. Carbapenems are an important class of antibiotics because they are safe and effective against MDR bacterial infections. Carbapenems have emerged as the standard-of-care for many MDR and other bacterial infections, but they have been available to date only intravenously for such indications.

  Based on our pre-investigational new drug application meeting, or pre-IND meeting, with the U.S. Food and Drug Administration, or FDA, and subject to our receiving favorable results from our Phase 1 clinical trial of SPR994 acceptable to the FDA, we believe we will be able to progress directly to a pivotal Phase 3 clinical trial of SPR994 for the treatment of cUTI. We filed a Clinical Trial Notification, or CTN, in Australia in September 2017 and initiated in October 2017 a Phase 1 dose-selection clinical trial of SPR994. A CTN enables conduct of clinical trials in Australia similar to an investigational new drug application, or IND, in the United States. We expect to report top-line data from this trial in mid-2018. We intend to request a meeting with the FDA to discuss the clinical trial protocol during the second half of 2018. Following our discussions with the FDA, we expect to initiate a pivotal Phase 3 clinical trial of SPR994 for the treatment of cUTI around year-end 2018 in support of a new drug application, or NDA.

  Our clinical strategy is supported by extensive safety data underlying tebipenem's regulatory approval in Japan and long-standing use in Japan for common pediatric infections. Approximately 1,100 subjects, including approximately 741 adults, have been dosed with tebipenem at a range of doses in clinical and pharmacologic studies. We have rights to use all clinical data generated by Meiji, including two exploratory Phase 2 trials that were conducted in Japan in patients with cUTI, the first indication in which we intend to study SPR994. Further, we have received Qualified Infectious Disease Product, or QIDP, designation from the FDA for SPR994 for the treatment of cUTI, community-acquired bacterial pneumonia, or CABP, and moderate to severe diabetic foot infections, or DFI, which provides priority review of SPR994 for regulatory approval by the FDA. The QIDP designation for SPR994, however, does not guarantee a faster development process or ensure FDA approval.

  We have global commercialization rights to SPR994, except in certain contractually specified Asian countries. We believe that our intellectual property portfolio will provide SPR994 protection globally, including in the United States and Europe, through 2038.

- ***Potentiator Platform (SPR741 and SPR206): Innovative Platform Designed to Target MDR Gram-Negative Bacterial Infections***. Our Potentiator Platform molecules are designed to treat Gram-negative bacterial infections through the molecules' interactions with the bacteria's outer cell membrane as a monotherapy or by co-administering our Potentiator Platform molecules with existing antibiotics, thereby making the existing antibiotics more effective by clearing a path for them to enter and kill the bacteria. Gram-negative bacteria are a subset of bacterial organisms distinguished by the presence of an outer cell membrane. Our Potentiator Platform relies on our unique chemical and

biological insights that enable us to design molecules that specifically increase the permeability of this outer cell membrane. Specifically, our Potentiator Platform molecules utilize a mechanism of action whereby they interact with constituents of the outer cell membrane called lipopolysaccharides, or LPS, resulting in a loss of outer membrane integrity and increased permeability, thereby potentially allowing antibiotics that were previously excluded to enter the Gram-negative bacteria where they become active or in the case of our direct acting molecules to exhibit potent activity alone against these bacteria. Since we began work on our Potentiator Platform in 2015, we have generated two development-stage product candidates: SPR741 and SPR206.

We have two Potentiator Platform product candidates – SPR741, our combination IV-administered agent that has demonstrated *in vitro* the ability to expand the spectrum and increase the potency of a co-administered antibiotic; and SPR206, our direct acting IV-administered agent that has demonstrated *in vitro* activity alone. Both have demonstrated potency against Gram-negative bacteria, including organisms identified by the Centers for Disease Control and Prevention, or the CDC, and the World Health Organization, or the WHO, as urgent and serious threats to human health.

SPR741 has demonstrated an ability to potentiate over two dozen existing antibiotics by expanding their activity against Gram-negative pathogens. While previous attempts by others to develop agents that interact with the bacteria's outer membrane using the mechanism of action employed by SPR741 have, to our knowledge, failed in preclinical testing and Phase 1 clinical trials due to safety concerns, data from our Phase 1 single-ascending dose, or SAD, and multiple-ascending dose, or MAD, clinical trial of SPR741 demonstrate it was generally well tolerated at single doses up to and including 800 mg and at doses up to and including 600 mg every 8 hours for 14 days.

In late November 2017, we initiated our Phase 1b drug-drug interaction clinical trial of SPR741 in the United Kingdom. The Phase 1b trial enrolled 27 healthy volunteers to evaluate SPR741 as a single dose in combination with compounds from the beta-lactam class of antibiotics, including cephalosporins (ceftazidime), monobactams (aztreonam) and beta-lactams/beta-lactamase inhibitors (piperacillin/tazobactam). The trial was designed to assess the impact, if any, on the standalone pharmacokinetics of SPR741 or the standalone pharmacokinetics of the beta-lactam combination drug when the two are dosed together as a single dose. We anticipate top-line data from this Phase 1b trial during the second quarter of 2018.

In addition, we continue to progress the development of our direct-acting Potentiator Platform molecules, exemplified by our product candidate SPR206. SPR206 is designed to also have antibiotic activity as a single agent against MDR and extremely drug resistant, or XDR, bacterial strains, including variants isolated in *Pseudomonas aeruginosa, Acinetobacter baumannii* and carbapenem-resistant *Enterobacteriaceae*. We are currently testing SPR206 in a good laboratory practice, or GLP, preclinical toxicology study. Recent data from this study suggest a potency and safety profile for SPR206 that may be superior to SPR741, as well as a potentially faster path to market than SPR741 because SPR206 can be developed as a single agent.

We believe that our intellectual property portfolio for SPR741 will provide SPR741 protection globally, including in the United States and Europe, through 2038. Additionally, we have multiple patent applications pending for SPR206 that we believe will provide SPR206 protection globally, including in the United States and Europe, through 2035.

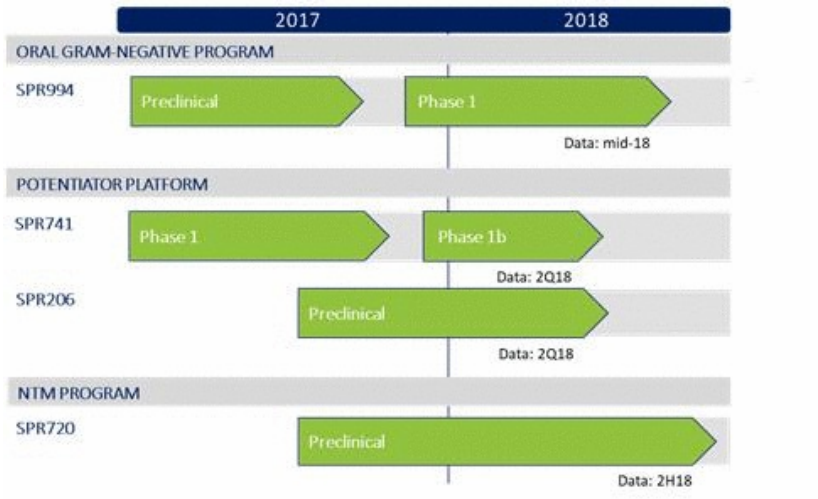
- ***SPR720: Novel Antibiotic with Potential to be the First Approved Oral Treatment for Pulmonary Non-tuberculous Mycobacterial Infections, an orphan infectious disease***. SPR720 is our novel oral therapy product candidate designed for the treatment of NTM infection. Lung infections caused by NTM are rare, and occur most frequently in patients with compromised immune systems, including human immunodeficiency virus, or HIV, or respiratory conditions, such as cystic fibrosis, chronic obstructive pulmonary disease, asthma and bronchiectasis. The annual prevalence of NTM infection is increasing at an estimated rate of 8% per year. The current treatment for NTM infection is lengthy and involves combination therapy, often including three or more antibiotics, including some parenterally administered. None of these treatments are 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 and mortality is high. We believe SPR720, if successfully developed, has the potential to be the first oral antibiotic approved for the treatment of this debilitating orphan disease. *In vitro* and *in vivo* studies have demonstrated the potency of SPR720 against a range of bacteria causing NTM infection, including *Mycobacterium abscessus*, a highly resistant strain causing infections with high mortality.

  SPR720 is currently in preclinical development. We are conducting 28-day and 31-day toxicity studies in rats and non-human primates in accordance with GLP regulations. We have also observed activity as good as or better than positive controls in in vitro and in vivo studies, including in an acute murine pneumonia model of infection caused by Mycobacterium abscessus. We are currently testing SPR720 in animal studies to assess activity across other pathogens of interest. Pending positive results from our additional toxicity studies, we plan to initiate a Phase 1 clinical trial of SPR720 in the first half of 2019.

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

Our Pipeline

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



Portfolio Prioritization

After we receive results from the Phase 1b clinical trial of SPR741 and our ongoing preclinical toxicology study of SPR206, we intend to prioritize our product candidates for further clinical development. Our decision will be based on which program we believe represents the best opportunity for us within an optimal timeframe, factoring in the choices we must make to prioritize the opportunities within our portfolio and to best deploy our capital resources. Accordingly, for the balance of 2018, our internal operational plans and budget and our estimate of our cash runway being sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2019 are based on us funding the development of SPR994 and SPR720 and either SPR206 or SPR741 during that period. We may seek partnering opportunities or other non-dilutive funding for further clinical development of the potentiator candidate we elect to deprioritize.

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:

- ***Rapidly advance our lead product candidate SPR994 through clinical development and regulatory approval***. We initiated a Phase 1 dose-selection clinical trial of SPR994 in Australia in October 2017, and we expect to report top-line data from this trial in mid-2018. Following completion of this trial, leveraging data and know-how we have licensed from Meiji, we intend to request a pre-Phase 3 meeting with the FDA in late 2018. Following our discussions with the FDA, we expect to submit an IND and initiate the pivotal Phase 3 clinical trial of SPR994 for the treatment of cUTI around year-end 2018 in support of an NDA. In addition to cUTI, we believe SPR994 has the potential to treat other serious and life-threatening infections.
- ***Advance a product candidate from our Potentiator Platform through clinical development and regulatory approval, either through a collaboration or with non-dilutive funding (or both), and advance our other product candidates***. Both product candidates within our Potentiator Platform are advancing, and we expect to bring forward one of our Potentiator Platform product candidates for further clinical testing in 2018. Regarding SPR741, we recently completed a Phase 1, two-part, randomized, double-blind, placebo-controlled, dose-escalation clinical trial. Regarding SPR206, recent preclinical data suggest a potency and safety profile that may be superior to SPR741, as well as a potentially faster path to pivotal trials than SPR741, because SPR206 can be developed as a single agent. The SAD and MAD data from the SPR741 clinical trial indicated that SPR741 was generally well tolerated at single

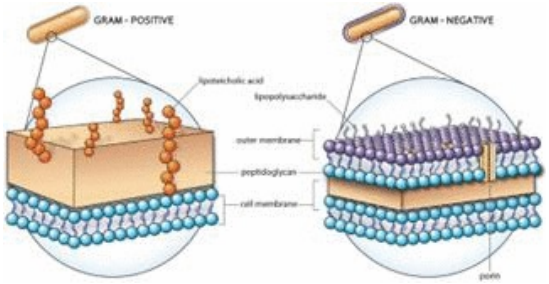
doses up to and including 800 mg and at doses up to and including 600 mg every 8 hours for 14 days. We submitted a CTA in the United Kingdom in October 2017 and, we initiated our Phase 1b drug-drug interaction clinical trial of SPR741 in the United Kingdom during the fourth quarter of 2017. Based on the results of the SPR741 Phase 1b trial and results from a GLP toxicology study for SPR206 we expect to prioritize which of these product candidates we will bring forward as our lead clinical Potentiator product candidate. We intend to continue to advance our other product candidates, including SPR720, through preclinical and clinical development.

- ***Maximize the value of our Potentiator Platform 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 optimal to develop and commercialize one or more of our Potentiator product candidates through partnering opportunities. These may include global 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. We believe this approach will 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 are currently receiving funding support of up to an aggregate of $10.1 million from 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 the Biomedical Advanced Research and Development Authority, or 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.
- ***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. 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. 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.
- ***Establish global commercialization and marketing capabilities***. We have global commercialization rights to all of our product candidates, with the exception of SPR994 in certain contractually specified Asian 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 infection.*** We believe there is a significant opportunity to develop products for underserved "orphan" infectious disease areas, such as NTM infection. These markets offer the attributes of fewer branded or generic competitors as well as chronic therapy. Our drug candidate SPR720 has the potential to be the first oral antibiotic approved for the treatment of pulmonary non-tuberculous mycobacterial infections. We may seek to acquire other product candidates for other underserved, debilitating orphan infectious diseases.

The Problem: Antibiotics and Drug Resistance

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. 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 people 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, meaning 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 various *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.

Our Product Candidates Have the Potential to Overcome Limitations of Available Treatment Options

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

- ***SPR994 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***. 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. However, currently there are no oral antibiotics commercially available that can reliably be used in adults with MDR Gram-negative infections. SPR994 is an orally administrable tablet that we believe has the potential to treat such infections in both the community and hospital settings, thereby preventing certain hospitalizations and enabling patients to transition to oral treatment.
- ***SPR741 and SPR206 are designed to address the decline of novel and effective IV-administered antibiotics to treat MDR Gram-negative infections in the hospital setting***. First-line empiric antibiotics, such as levofloxacin, ceftazidime and piperacillin-tazobactam, have experienced diminished utility as the number of bacterial strains resistant to these antibiotics 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. We believe that SPR741 has the potential to address the need for more effective treatments against MDR Gram-negative bacterial infections by expanding the spectrum and potency of existing antibiotics, including formerly inactive antibiotics. We believe that SPR206 has the potential to address this need as a single agent.
- ***SPR720 is designed to be the first oral treatment for an orphan disease, 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 effectiveness *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.

Our Product Candidates

SPR994 (Tebipenem Pivoxil Extended Release)

Our lead product candidate, SPR994, is designed to be a broad-spectrum oral carbapenem for use in adults to treat MDR Gram-negative infections. Currently, there are no commercially available oral carbapenems for use in adults, and we believe SPR994 has the potential to address this unmet need. 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. SPR994 is an oral extended-release tablet formulation of tebipenem. Tebipenem was approved in 2009 in Japan for sale under the name Orapenem for pediatric use in common infections, including pneumonia, otitis media and sinusitis. It has been sold by Meiji in Japan as a granule presentation for children, and is combined with food and dosed twice per day. To accelerate our clinical development of SPR994, in June 2017 we exclusively licensed certain data and know-how from Meiji and a global pharmaceutical company, which we refer to as Global Pharma, which we intend to use to support our clinical development of SPR994. The FDA has designated SPR994 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. The QIDP designation for SPR994, however, does not guarantee a faster development process or ensure FDA approval. We believe, if approved, that SPR994, which incorporates our proprietary formulation technology and benefits from know-how and data we have licensed from Meiji, has the potential to further increase the clinical demand for the carbapenem class of antibiotics.

We have global commercialization rights to SPR994, except in certain contractually specified Asian countries. If SPR994 is approved for treatment of cUTI, CABP or DFI, the QIDP designation for SPR994 will extend by an additional five years any non-patent exclusivity period awarded for SPR994 in the United States, such as a five-year New Chemical Entity, or NCE, exclusivity granted under 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 SPR994, which includes multiple patent applications pending, will provide SPR994 protection globally, including in the United States and Europe, through 2038.

Potential Advantages of SPR994

We believe that the following key attributes differentiate SPR994 from other antibiotics targeting MDR Gram-negative infections. We believe these attributes have the potential to make SPR994 a safe and effective treatment for cUTI and other serious and life-threatening infections for which we may develop SPR994.

- ***Potential to be the first oral carbapenem in adults***. SPR994 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, SPR994 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.
- ***Favorable safety, efficacy and tolerability profile suggested by clinical studies 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 1,100 subjects have been dosed with the active pharmaceutical ingredient of SPR994, tebipenem, in clinical and pharmacologic studies during development of this drug by Meiji and Global Pharma in Japan. This data set includes 741 adults, including 88 patients with cUTIs, the initial indication for which we plan to develop SPR994. In each case tebipenem has demonstrated a favorable safety, pharmacokinetic and tolerability profile.
- ***Broad spectrum of activity against a variety of MDR Gram-negative, Gram-positive and anaerobic bacteria, with a potency consistent with certain IV-administered carbapenems***. In *in vitro* studies, SPR994 displayed potent antibiotic activity against Gram-negative bacteria, including *E. coli* producing extended spectrum beta lactamases, or ESBLs, and ESBL-producing *Klebsiella pneumoniae.* ESBL-producing bacteria are Gram-negative bacteria that hydrolyze, or break down, cephalosporins and render them ineffective for treatment. ESBL-producing pathogens are associated with poor clinical outcomes in severe infections. Further, the potency of SPR994 against *Enterobacteriaceae* has been observed to be similar to IV-administered ertapenem (or ETP) and imipenem (or IMI). As a result, we believe that SPR994 has the potential to be used for the treatment of cUTI and other serious and life-threatening infections caused by resistant Gram-negative pathogens.
- ***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 SPR994 may enable patients who begin IV-administered treatment for ESBLs in the hospital setting to transition to oral dosing of SPR994 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 SPR994 also significantly differentiate SPR994 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 SPR994 and levofloxacin, the most widely used fluoroquinolone. As shown below, SPR994 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)
SPR994	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. In Japan, Orapenem (tebipenem pivoxil) does not have a black box warning and has been studied in approximately 1,100 subjects. We believe SPR994 could become a potential alternative to oral fluoroquinolones based on its safety and efficacy profile.

Significant Market Opportunity for SPR994

Given the observed activity of SPR994 against different bacteria, we view the market opportunity for SPR994, if approved, to be substantial, including for the following uses:

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

UTIs are among the most common bacterial diseases worldwide, with significant clinical and economic burden. 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.

QuintilesIMS 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 SPR994 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 SPR994 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. Our initial study for SPR994 will focus 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.

Additional use may be seen in treating patients hospitalized with complicated Gram-negative infections, such as complicated intra-abdominal infections, or cIAI, hospital-acquired, or nosocomial, pneumonia and blood stream infections as they are discharged from the hospital.

SPR994 Clinical Development Program

Based on our pre-IND meeting with the FDA, we initiated a Phase 1 pharmacokinetics and safety clinical trial in Australia of SPR994 in October 2017, and expect to report top-line data from this trial in mid-2018. Following completion of this trial to select a dose for pivotal trials, we intend to request a pre-Phase 3 meeting with the FDA to confirm that no additional clinical trials or preclinical studies are required prior to initiating a Phase 3 clinical trial. Subject to feedback from the FDA, and using know-how we have licensed from Meiji, we plan to obtain agreement on the clinical trial protocol in late 2018 and expect to initiate the pivotal

Phase 3 clinical trial of SPR994 for the treatment of cUTI around year-end 2018 under an IND. We anticipate that the data from this study will form the basis for the clinical trial data package that will support an NDA.

The FDA has designated SPR994 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 SPR994, however, does not guarantee a faster development process or ensure FDA approval. Further, if SPR994 is successfully developed and approved for the treatment of cUTI, CABP or DFI, the FDA's QIDP designation for SPR994 should extend any non-patent exclusivity period awarded to SPR994 in the United States for five years, such as a five-year New Chemical Entity data exclusivity granted under The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act.

SPR994 Phase 1 Clinical Trial

We filed a CTN in Australia in September 2017 and initiated in October 2017 a Phase 1 clinical trial in Australia of SPR994 in approximately 60 healthy volunteers. A CTN enables conduct of a clinical trial in Australia similar to the manner that an IND enables such a study in the United States. The Phase 1 clinical trial is evaluating several oral tablet formulations of SPR994 designed to optimize exposure. The trial consists of SAD cohorts and multiple dose cohorts. The objective of the trial is primarily dose selection for our planned Phase 3 trial and includes determination of pharmacokinetics, safety and tolerability for up to 14 days and food effect. In particular, the focus of the SAD cohort is to assess the safety and probability of target attainment (killing of target pathogens). The focus of the MAD cohorts is on dose and schedule, specifically, determining how dose drives bacterial clearance over time. We expect to use data from the trial to refine a pharmacokinetic/pharmacodynamic model to establish an *in vitro/in vivo* relationship to support dose and schedule administration for our planned pivotal Phase 3 clinical trial based on drug concentration and inter-patient variability. We expect to report top-line data from the Phase 1 clinical trial in mid-2018.

Planned Pivotal SPR994 Phase 3 Clinical Trial

Based on our pre-IND meeting with the FDA, we believe that results from our Phase 1 clinical trial of SPR994, together with nonclinical studies, PK/PD, and other supporting data, will be acceptable to FDA to allow us to commence a pivotal Phase 3 clinical trial of SPR994 under a U.S. IND. After we report top-line data from our Phase 1 clinical trial, we plan to request a pre-Phase 3 meeting with the FDA to confirm that no additional clinical trials or preclinical studies are required prior to initiating our Phase 3 clinical trial. Subject to feedback from the FDA, we plan to submit an IND and agree upon the clinical trial protocol in late 2018 and expect to initiate the pivotal Phase 3 clinical trial of SPR994 for the treatment of cUTI and acute pyelonephritis around year-end 2018. Clinical trial applications will also be submitted in Europe and other regions, as needed, to support study enrollment. Our planned pivotal Phase 3 clinical trial of the efficacy and safety of SPR994 is currently designed as a double-blind, double-dummy trial to compare SPR994 with an existing standard of care antibiotic in approximately 1,100 patients randomized 1:1 in each arm. We believe that the primary endpoint of the trial will be non-inferiority versus a standard of care antibiotic, with a 10% non-inferiority margin. We intend to commence our pivotal Phase 3 clinical trial with a lead-in cohort with intensive pharmacokinetics sampling in order to analyze exposure prior to enrolling the majority of the Phase 3 clinical trial cohort. In this Phase 3 trial, the primary efficacy endpoint is clinical cure and microbiological eradication in the microbiological intent-to-treat population per U.S. FDA guidance for cUTI trials. We will also assess the trial for the primary efficacy endpoint of microbiological eradiation in the microbiologically evaluable population per the European regulatory requirements, under a separate statistical analysis plan of the same datasets.

Following receipt of top-line data from this pivotal Phase 3 clinical trial, with requisite safety data, drug-drug interaction studies and other studies, we intend to submit to the FDA an NDA for SPR994 to treat cUTI including acute pyelonephritis. These data, if positive, may also support marketing applications in other global regions. We also intend to reach an agreement with the FDA on a Pediatric Study Plan and initiate development of SPR994 in pediatrics for cUTI upon receipt of top-line data in adult patients.

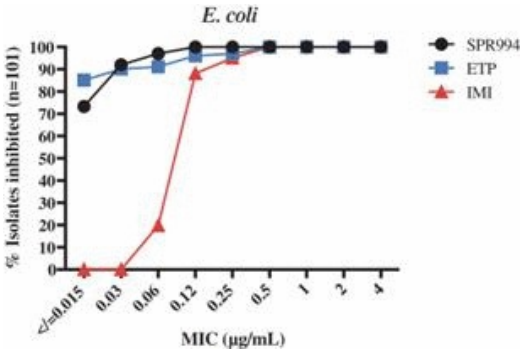
Data Supporting the Use of SPR994 for the Treatment of cUTI

We have tested SPR994 *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. In addition, approximately 1,100 subjects have been dosed with tebipenem 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 SPR994. 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.

In vitro Activity Against MDR Enterobacteriaceae

Results from multiple susceptibility testing studies against MDR Enterobacteriaceae demonstrate that SPR994 remained potent against strains resistant to several other classes of antibiotics, including aminoglycosides and fluoroquinolones. In these studies, we measured the potency, or MIC, of each drug by determining the concentration of drug required to inhibit the growth of 50% and 90% of the isolate set (i.e., the MIC50 or MIC90). The graph below depicts the *in vitro* activity of SPR994 compared to two commercially available intravenously delivered antibiotics commonly used to treat cUTI against a large number of clinical isolates, namely Invanz (ertapenem, or ETP) from Merck and generically available imipenem, or IMI.

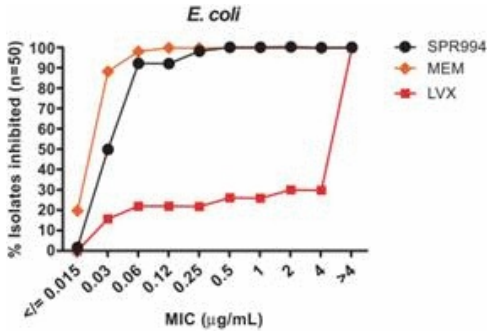
SPR994 Activity Against Contemporary Isolates of *E. coli*



SPR994 has showed MIC50 and MIC90 values of less than or equal to 0.015 µg/mL and 0.03 µg/mL, which compare favorably (i.e., at or below) to the values obtained by competitive agents ertapenem and imipenem.

Regarding a more resistant set of *E. coli* isolates, including fluoroquinolone-resistant strains, SPR994 again showed *in vitro* activity similar to commercially available intravenously delivered drugs such as Merrem (meropenem, or MEM), and better than levofloxacin, or LVX, as shown in the graph below.

SPR994 is Active Against *E. coli*, Including Fluoroquinolone-Resistant Isolates



SPR994 has also shown activity in preclinical *in vitro* studies against a wide variety of ESBL-producing E. coli and ESBL-producing K. pneumoniae strains, as highlighted in the table below.

SPR994 Has Potent Activity Against A Variety of ESBL Enzymes
***In vitro* Activity of SPR994 and Comparator Antibiotics against Clinical Isolates**

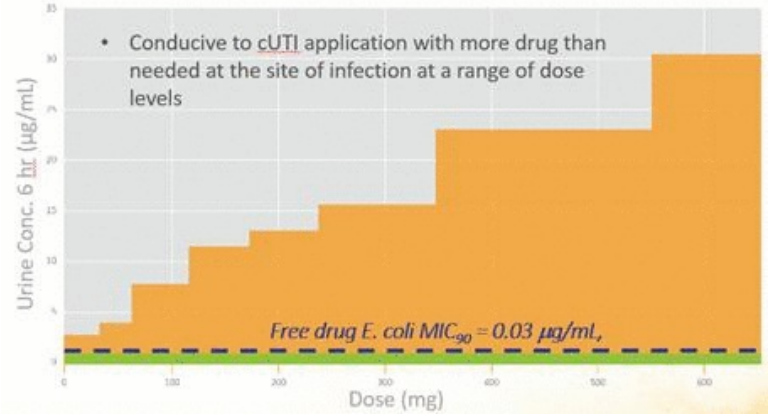
Organism	ESBL Enzyme Content	N	MIC Range (µg/ml)			
			SPR994*	Meropenem	Amoxicillin /Clavulanic Acid	Levofloxacin
E. coli	CTX-M (group 1)	13	0.03 – 0.06	0.015 – 0.03	1 – 32	>4
	CTX-M (group 9)	6	0.015 – 0.03	0.015 – 0.03	4 – 16	>4
	CTX-M (group 9), TEM (wild type)	1	0.03	0.03	16	>4
	CMYII	3	0.03 – 0.12	0.03 – 0.06	64	0.03 – >4
	CMYII, TEM (wild type)	3	0.03 – 0.06	0.03	32	0.06 – >4
	CTX-M (group 1), TEM (wild type)	6	0.015 – 0.03	0.03	16 – 32	2 – >4
	SHV (ESBL), TEM (wild type)	2	0.03, 0.06	0.03, 0.06	16	>4
K. pneumoniae	SHV (ESBL), SHV (wild type)	2	0.03, 0.12	0.03	4, 32	>4
	CTX-M (group1), SHV (wild type), TEM (wild type), CTX-M-55/57	1	0.03	0.03	16	>4
	CTX-M (group1), SHV (wild type), CTX-M-15, OXA-1/30-like	1	0.03	0.06	16	2
	CTX-M (group9), SHV (ESBL), SHV (wild type), TEM (wild type),SHV-1	1	0.06	0.03	16	>4
	FOX, SHV (wild type)	1	0.03	0.03	32	0.5
	CMYII, SHV (wild type)	1	0.03	0.06	64	0.06
	CTX-M (group1), SHV (ESBL), SHV (wild type), CTX-M-15, OXA-1/30, SHV-5	1	0.12	0.06	16	>4
	DHA, SHV (wild type), TEM (wild type)	1	0.25	0.06	32	0.5
			MIC > 2 µg /mL	MIC 1-2 µg /mL		MIC < 1 µg /mL

We believe these data show the ability of orally available SPR994 to deliver similar activity to comparative IV-administered agents.

Tebipenem Phase 1 Clinical Trial Data Support Development of SPR994 for the Treatment of cUTI

Tebipenem was also tested by Meiji in healthy volunteers to determine urinary concentrations as a predictor of efficacy in the cUTI population. Results from this single-ascending dose study are shown in the graph below.

Single-Ascending Dose Calculated Urine Levels of Tebipenem



In early clinical studies in Japan, healthy volunteers received doses up to 600 mg/day. At each dose level, and in a dose dependent manner, the urine concentration of tebipenem exceeded the MIC90 for E. coli of 0.03 µg/ml (defined as the level that is expected to inhibit 90% of E. coli isolates).

A food-effect clinical study was performed to evaluate the impact of meals or dairy products on tebipenem-pivoxil granule pharmacokinetics. The study showed comparable plasma AUC (a measure of drug exposure over time) and urinary excretion rates of tebipenem pivoxil among the study's subjects in both the fed and fasted states. The effect of a meal or dairy products on tebipenem absorption was observed to be limited, and no adverse safety or tolerability effects were observed in dosing in the fed state.

Meiji Phase 2 Clinical Trial Data of Tebipenem in cUTI

Meiji and Global Pharma 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 at doses of 100 mg administered three times daily, or 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 at doses of 250 mg administered BID (500 mg Group) and 300 mg administered TID (900 mg Group) for seven days in patients with cUTI. 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).

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 support our plan to develop SPR994 in 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 in Meiji Phase 2 Trials in cUTI

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."

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 SPR994 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 1,100 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 serum carnitine concentrations.

In these studies, tebipenem pivoxil was generally safe and 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 (also a pivoxil prodrug), 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 serum 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. 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.

A total of 3,547 cases were enrolled into the study, and the analysis was conducted using 3,540 cases for which it was possible to recover the questionnaires. Of these 3,540 cases, a total of 3,331 cases were used in the safety analysis, 2,844 cases were used in the efficacy analysis, 2,769 cases were used in the clinical efficacy analysis, and 461 cases were used in the bacteriological efficacy analysis. The incidence of adverse drug reactions was 9.97% (332/3,331 cases), and the primary adverse drug reactions were “gastrointestinal disorders” such as diarrhea, which occurred in 317 cases (9.52%). “Diarrhea” occurred in 313 cases (316 instances). All of these events were non-serious, and 94.9% (297/313 cases) showed recovery or remission.

A clinical study 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.

Our Potentiator Platform (SPR741 and SPR206)

We have two product candidates in our Potentiator Platform, SPR741 and SPR206. Both product candidates are IV-administered derivatives of Polymyxin B, or PMB. Both have demonstrated *in vitro* activity against Gram-negative bacteria, including organisms identified by the CDC and the WHO as urgent and serious threats to human health. There are two primary differences between these two product candidates. SPR741 has minimal antibacterial activity as a single agent and requires combination therapy with a companion antibiotic to demonstrate antimicrobial potency. SPR741 also has demonstrated activity primarily against MDR Gram Negative organisms such as *Enterbacteriaceae* and against some strains of *Acinetobacter baumanii* depending on its combination partner. SPR206 is active as a single agent and exerts potency with and without a partner. SPR206 also has a broad spectrum of activity including all the strains SPR741 covers, as well as expanded coverage of carbapenem-resistant *Pseudomonas aeruginosa*, carbapenem-resistant *Acinetobacter baumanii* and carbapenem-resistant *Enterobacteriaceae*.

We have completed a Phase 1, two part, randomized, double-blind, placebo-controlled, dose-escalation trial of SPR741. We initiated our Phase 1b drug-drug interaction clinical trial of SPR741 in the United Kingdom during the fourth quarter of 2017. The Phase 1b trial enrolled 27 healthy volunteers to evaluate SPR741 as a single dose in combination with compounds from the beta-lactam class of antibiotics, including cephalosporins (ceftazidime), monobactams (aztreonam) and beta-lactam/beta-lactamase inhibitors (piperacillin/tazobactam). The trial was designed to assess the impact, if any, on the standalone pharmacokinetics of SPR741 or the standalone pharmacokinetics of the beta-lactam combination drug when the two are dosed together as a single dose. We anticipate top-line data from this Phase 1b trial during the second quarter of 2018.

We believe that our intellectual property portfolio for SPR741, which includes multiple issued patents and patent applications pending, will provide SPR741 protection globally, including in the United States and Europe, through 2038. Additionally, we have multiple patent applications pending for SPR206 that we believe will provide SPR206 protection globally, including in the United States and Europe, through 2035.

How Our Potentiator Platform Molecules Are Designed to Work

Gram-positive and Gram-negative bacteria are classified by the lab staining test known as the "Gram stain", but their nature is due to structural differences in their cell envelope, with Gram-positive bacteria surrounded by a single lipid membrane and a thick cell wall and Gram-negative bacteria encircled by two lipid membranes, an inner membrane and an outer membrane, with a thinner cell wall in between. 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 to reduced potency of many agents in treating Gram-negative bacterial infections. Each membrane in Gram-negative bacteria excludes different types of chemical entities, requiring Gram-negative active antibiotics to be specifically designed to permeate both membranes. Gram-negative bacteria include *Pseudomonas aeruginosa, Acinetobacter baumannii*, and the *Enterobacteriaceae*, a family of related organisms that includes *E. coli, Klebsiella pneumoniae, Enterobacter, Salmonella,* and *Shigella species*.

Advantages of our Potentiator Platform

We believe that the following key attributes of our Potentiator Platform generally have the potential to support the clinical utility and commercial value of our Potentiator Platform for the safe and effective treatment of serious infections:

- ***Potential to Expand the Potency of Standard-of-Care Antibiotics***. We believe SPR741and SPR206 have the potential to expand the potency of standard-of-care antibiotics by restoring and expanding their Gram-negative activity, thereby improving therapeutic outcomes, decreasing physicians' reliance on drugs of last resort and encouraging improved antibiotic stewardship.
- ***SPR741 was demonstrated to be well tolerated in Phase 1 studies***. Data from our Phase 1 SAD and MAD clinical trial of SPR741 demonstrate SPR741 was generally well tolerated at single doses up to and including 800 mg and at doses up to and including 600 mg every 8 hours for 14 days.
- ***SPR206 may potentially be a safe and potent IV-administered direct-acting agent***. Like SPR741, our Potentiator Platform candidate SPR206 is designed to interact with LPS to disrupt the outer membrane. However, SPR206 is also designed to have direct antibiotic activity, while retaining potentiator activity, including activity against *Pseudomonas* and *Acinetobacter*. 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.

Significant Market Opportunity for SPR741 and SPR206, including Gram-Negative IV Market

The need for new antibiotics to treat CRE, CRAB and MDR PA is particularly acute, as together these represent among the top global threats in infectious disease. In February 2017, the WHO published a list of Gram-negative bacteria based on the urgency of need for new antibiotics: critical, high and medium priority. The most critical group includes MDR bacteria that pose a particular threat including *Acinetobacter*, *Pseudomonas* and various *Enterobacteriaceae* (including *Klebsiella*, *E. coli*, *Serratia*, and *Proteus*). These bacteria can cause severe and often deadly infections. As such, there is an acute need for new drugs to treat MDR Gram-negative bacteria. Currently approved products are increasingly ineffective against Gram-negative bacteria due to increasing resistance, resulting in limited treatment options for patients with MDR infections. Few new therapeutic agents have been approved or are in clinical development to treat infections caused by Gram-negative bacteria.

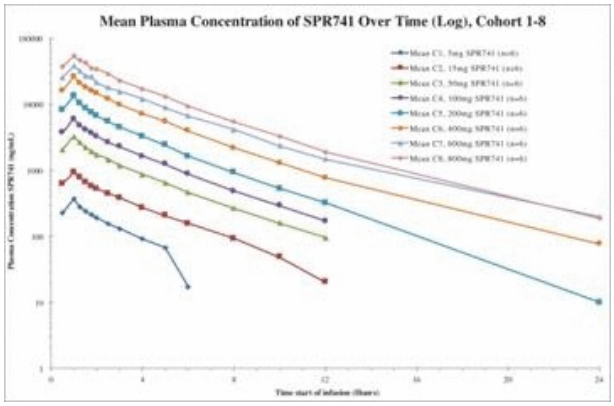
Acinetobacter *baumannii* is an opportunistic bacterial pathogen primarily associated with hospital-acquired infections. The recent increase in incidence, largely associated with infected combat troops returning from conflict zones, coupled with a dramatic increase in the incidence of MDR strains, has significantly raised the profile of this emerging opportunistic pathogen. It is estimated between 50,000 to 80,000 infections annually in the United States and approximately 63% of isolates are MDR. Mortality rates for patients with *Acinetobacter baumannii* have been reported as high as 43%. Currently the only drugs to treat these resistant organisms are polymyxins such as colistin, polymixyn B, or PMB, and tigecycline, or TIG, both of which have significant safety and tolerability issues. SPR206 would provide a much needed addition to the treatment of these very serious infections.

Pseudomonas is one of the most common Gram-negative organisms in the hospital setting. Incidence ranges from 13% in UTIs and as high as 25% in respiratory tract infections. Resistance to commonly used agents such as cephalosporins, piperacillin/tazobactam and quinolones ranges from 10% in the non-ICU setting to upwards of 35% in the ICU. Even more problematic is the increase in resistance to carbapenems, which is reported to be as high as 19% in the ICU. *Pseudomonas* is a serious cause of infection with morbidity and mortality rates of 18% to 61%. In preclinical studies to date, SPR206 has demonstrated potent activity across a broad range of resistant strains of *Pseudomonas aeruginosa*. There are limited treatment options available today to treat these resistant organisms.

CRE infections are associated with significant mortality, with up to 50% mortality observed in patients with bloodstream infections. With limited treatment options available for CRE infections, physicians have resorted to older drugs such as colistin or more recently drugs such as tigecycline and ceftazidime/avibactam. However, there is evidence that these antibiotics are failing patients. For example, in bloodstream infections due to carbapenemase-producing *Klebsiella pneumoniae*, all-cause mortality for treatment with colistin, tigecycline, or combinations of antibiotics that do not include a carbapenem active *in vitro* against the infecting isolate was reported to be 46%, 47%, and 37%, respectively. Recently, resistance to even these last-resort treatments has begun to be reported, further increasing the urgency for new therapeutic options.

SPR741—Phase 1 Clinical Trial and Clinical Development

Data from our Phase 1 SAD and MAD clinical trial show SPR741 administered intravenously in single doses up to and including 800 mg and multiple daily doses up to and including 600 mg every 8 hours for 14 days was generally well tolerated in healthy adult subjects. There were no deaths or serious adverse events. All subjects completed the study. As shown in the chart below, the pharmacokinetics observed in the SAD portion of the trial were dose linear and dose proportional with a half-life of between two and four hours, consistent with expectations from preclinical modeling. Similarly, the pharmacokinetics observed in the MAD portion of the trial were dose linear and dose proportional, with only minor accumulation noted in the top dose cohort (600 mg every 8 hours).



We initiated our Phase 1b drug-drug interaction clinical trial of SPR741 in the United Kingdom during the fourth quarter of 2017. The Phase 1b trial enrolled 27 healthy volunteers to evaluate SPR741 as a single dose in combination with compounds from the beta-lactam class of antibiotics, including cephalosporins (ceftazidime), monobactams (aztreonam) and beta-lactams/beta-lactamase inhibitors (piperacillin/tazobactum). The trial was designed to assess the impact, if any, on the standalone pharmacokinetics of SPR741 or the standalone pharmacokinetics of the beta-lactam combination drug when the two are dosed together as a single dose. We anticipate top-line data from this Phase 1b trial during the second quarter of 2018.

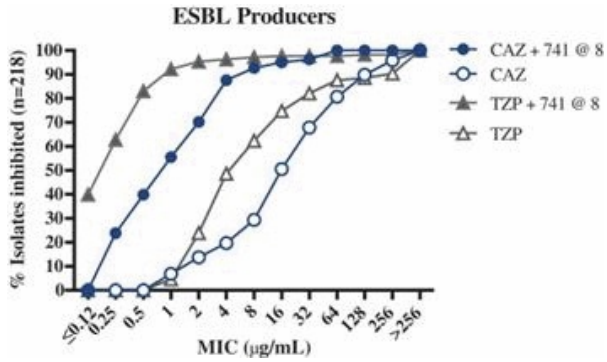
Our Potentiator Platform is funded in part with non-dilutive funding from the DoD and CARB-X, consisting of $1.9 million through March 31, 2018. We have global commercialization rights to SPR741, which has global patent protection extending through 2038.

In Vitro Activity of SPR741 Against MDR Gram-Negative Bacteria

Results from multiple susceptibility testing studies against suggest that SPR741 is capable of potentiating the activity of several classes of antibiotics, including some beta-lactams and macrolides. We ascertained the potential clinical profile of combinations of SPR741 against MDR Enterobacteriaceae encountered in the hospital setting by testing the combinations against a large number of clinical isolates collected from unique patients with different types of infections from hospitals around the world. In one such study,

we measured the ability of SPR741 to enhance the activity of ceftazidime, or CAZ, or piperacillin-tazobactam (Zosyn, or TZP) against a large collection of clinical isolates expressing the drug-resistant phenotype ESBL. In each case, as shown in the graph and summarized in the table below, SPR741 potentiated the activity of the antibiotics resulting in an MIC90 shift from 256 to 8 for CAZ and from 256 to 1 for TZP. We believe that this data demonstrates SPR741's ability to restore the combined antibiotic's therapeutic activity against a resistant strain of bacteria.

Potency of Piperacillin-Tazobactam and Ceftazidime with and without SPR741 in Global Set of Clinical Isolates Classified as ESBL Producers



MIC90 and % of Bacteria Susceptible to Piperacillin-Tazobactam and Ceftazidime with and without SPR741 in Global Set of Clinical Isolates Classified as ESBL Producers

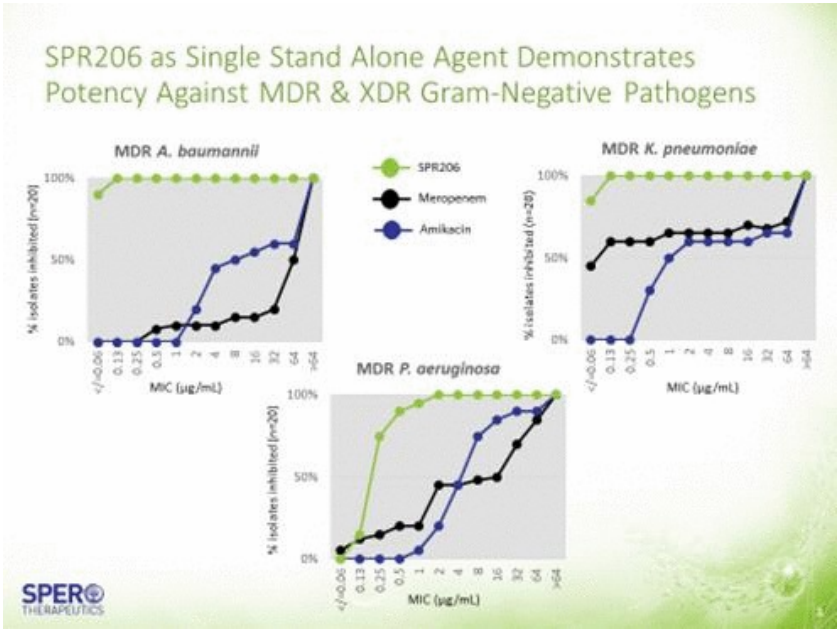
	MIC90 (mg/mL)	% Susceptible (1)
CAZ	256	20%
CAZ+SPR741	**8**	**88%**
TZP	256	75%
TZP+SPR741	**1**	**98%**

(1) Breakpoints for CAZ+SPR741 and TZP+SPR741 are defined by regulatory bodies only upon approval of NDA(s) and as such none exist today. As a surrogate, we have used the clinically approved breakpoints for CAZ and TZP to define anticipated susceptibility for our combinations.

SPR206—Development Plan

In Vitro Activity of SPR206 Against MDR Gram-Negative Bacteria

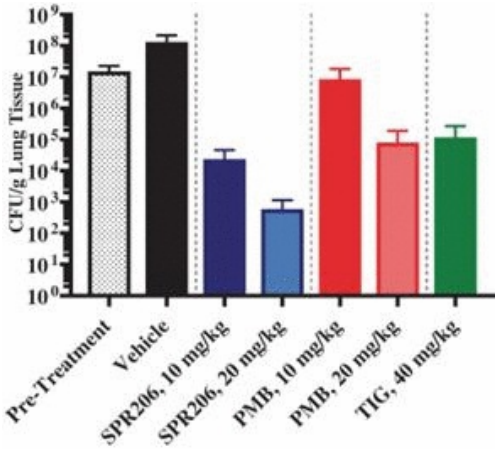
Results from multiple susceptibility testing studies against MDR Enterobacteriaceae suggests that SPR206 is capable potent activity against MDR Enterobacteriaceae, carbapenem resistant *Pseudomonas aeruginosa* and carbapenem resistant *Acinetobacter baumanii*.



In vivo Activity of SPR206 against Carbapenem-Resistant Acinetobacter baumannii

The activity of SPR206 against a carbapenem resistant strain of *Acinetobacter baumannii* exceeded the activity of polymyxin B (PMB) and tigecycline (TIG) in a mouse lung infection model as shown below.

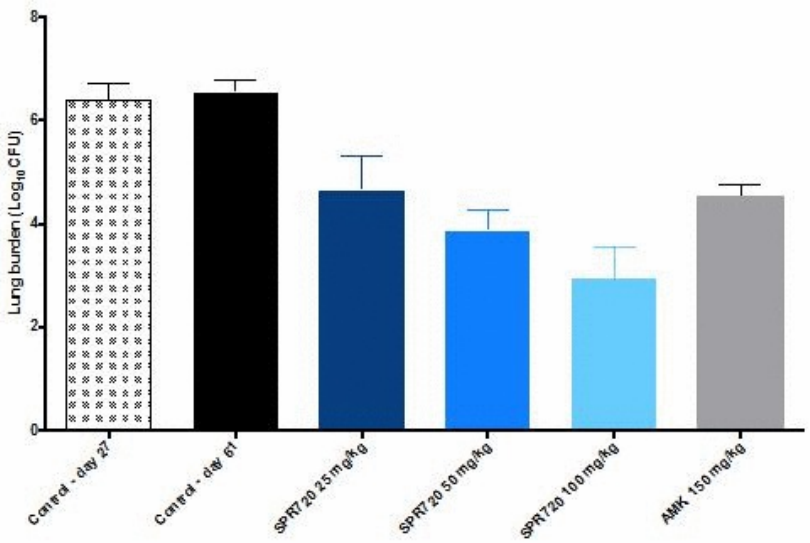
Activity of SPR206 vs. Comparators in a Mouse Lung Infection Model



Orphan disease, Pulmonary Non-Tuberculous Mycobacterial Infection Program

A third area of our focus is anti-infective orphan disease. We are developing SPR720, a novel mechanism of action therapeutic candidate for the treatment of NTM infection. SPR720 is designed to be the first novel, oral candidate to treat NTM infection. SPR720 is an orally available gyrase inhibitor. SPR720 has potent activity against most common NTM infection species, such as *M. avium*, *M. abscessus* and *M. kansasii*. As shown in the exhibit below, SPR720 shows dose responsive efficacy against difficult to treat, multidrug resistant pathogens, with better activity as compared to amikacin, or AMK, considered the positive control in this experiment.

Lung Infections in Multidrug Resistant Abscessus Strains



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

NTM infections occur in many different types of patients. NTM infections often occur 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 infection 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 infection has more than doubled since 1997. By comparison, the prevalence of tuberculosis in North America has declined.

There are currently no FDA-approved therapeutics indicated for NTM infections. Given the unmet medical need, there are regulatory incentives available to encourage drug development to address NTM infection. These include orphan drug designation, potential for breakthrough therapy status and QIDP designation. The current treatment for NTM infection is lengthy and involves combination therapy, often including three or more drugs including an injectable. 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 infection. While there are competitive compounds in late-stage development for NTM infection, 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 infection, and to enable refractory patients to regain a better quality of life. SPR720 is currently in preclinical development. We have conducted 28-day GLP toxicity studies in rats and non-human primates, and we are waiting for the final results of these studies. We have also observed activity as good as or better than positive controls in *in vitro* and *in vivo* testing, including in an infection model caused by *Mycobacterium abscessus and Mycobacterium avium*. Pending further evidence of *in vivo* activity and positive results from our additional toxicity studies, we plan to initiate a Phase 1 SAD/MAD clinical trial in healthy volunteers during the first half of 2019.

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 exploring and developing. We have certain obligations under these acquisition or licensing agreements, including diligence obligations and payments, that 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.

Meiji Agreements

To support our development of SPR994, 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 SPR994.

We retain exclusive rights to commercialize SPR994 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 SPR994. With Meiji, we have established a joint development committee for the management of the development of SPR994, 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 SPR994. In October 2017, we 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 SPR994. 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 SPR994 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 SPR994 for efficacy, safety, legal or business factors, and (ii) under certain circumstances arising out of the head license with Global Pharma.

Potentiator Platform Agreements

Northern License Agreement

In February 2015, our subsidiary, Spero Potentiator, Inc., or Spero Potentiator, entered into a license agreement, or the 2015 Northern License Agreement, with Northern Antibiotics Oy (Ltd.) of Finland pursuant to which Northern granted to Spero Potentiator an exclusive, worldwide, perpetual and irrevocable license to develop and commercialize certain licensed compounds under certain patents, patent applications and know-how of Northern. In exchange for such exclusive license, Spero Potentiator issued an equity interest in Spero Potentiator and entered into a subscription agreement and shareholders agreement with Northern. In June 2017, we repurchased Northern's minority equity interest in Spero Potentiator in exchange for a one-time nonrefundable upfront fee of $1.0 million immediately and agreed to pay Northern $0.1 million within five days of the consummation of our initial public offering, or IPO, which event occurred and which amount was paid in November 2017. We also amended and restated the 2015 Northern License Agreement, which, as amended, we refer to as the 2017 Northern License Agreement, to include certain contingent cash payments as described below. The 2017 Northern License Agreement has a perpetual term and no express termination rights.

Under the 2017 Northern License Agreement, Northern granted to Spero Potentiator an exclusive, perpetual, irrevocable, worldwide license to develop and commercialize certain licensed compounds under certain Northern patents, patent applications and know-how in consideration for one or more near-term milestone payments up to an aggregate of $2.5 million based on either clinical milestones or the completion of our IPO, which event occurred and which amount was paid in November 2017, and in consideration for up to an aggregate of $4.5 million upon receipt of marketing approval of SPR741 or other compounds licensed from Northern which, in either case, is approved to be co-administered with a different antibiotic agent. With Northern, we have established a joint development committee for the exchange of information and ideas regarding development of the licensed compounds, to monitor conduct of activities and to provide and receive updates regarding new inventions. In addition, we provide periodic reports to Northern describing the development and commercialization of the licensed compounds, including SPR741.

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 pay a total of up to $5.8 million upon the achievement of specified clinical and regulatory milestones and to pay £5.0 million ($6.7 million as of December 31, 2017) 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.

In addition, Spero holds a NIAID contract that partially funds the next-generation potentiating agent development program. That contract was novated from CAI to Spero in December 2017. If NIAID exercises future contract options and we receive further funding from NIAID, then we will pay a portion of the proceeds to PBB pursuant to the Cantab Agreement.

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. 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

We have commitments of up to an aggregate of $10.1 million in non-dilutive funding from NIAID, the DoD and CARB-X. As noted above, our Potentiator Platform program is partially funded by a $1.5 million award from the DoD and an award of $1.9 million from CARB-X. The DoD funding supports next-generation Potentiator Platform discovery and screening of SPR741 partner antibiotics. The CARB-X award supports screening and selection of SPR741 partner antibiotics (with the exception of azithromycin) with the goal of taking one SPR741/partner combination through IND-enabling studies, culminating in the completion of a Phase 1 clinical trial. Our NIAID 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. Finally, NIAID is providing up to $5.7 million of funding for our next-generation Potentiator Platform molecules.

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 SPR994 and Other Compounds Under Development

We have patent applications directed to the composition of matter, formulation and/or use of SPR994, SPR741, SPR206 and SPR720 pending in the United States, Europe, Japan and other countries.

Oral Carbapenem (SPR994)

Our SPR994 program contains two pending U.S. provisional applications and one patent cooperation treaty, or PCT, application covering novel preparations of tebipenem pivoxil as of December 31, 2017, all wholly owned by us. The provisional patent applications will be converted to Patent Cooperation Treaty, or PCT, applications within one year of their filing dates. U.S. and foreign patents issuing from our tebipenem pivoxil patent applications will have statutory expiration dates of December 2037 and February 2038. Patent term adjustments or patent term extensions could result in later expiration dates.

Potentiator Platform (Including SPR741)

The intellectual property portfolio for our Potentiator Platform contains patent applications and issued patents directed to composition of matter for SPR741 and analogs thereof, composition of matter with different structural features, combinations of SPR741 or other potentiators with other anti-bacterial compounds, and methods of use for these novel compounds and compositions. As of December 31, 2017, we owned or were exclusively licensed eight U.S. patents and one U.S. provisional application; 94 foreign patents and nine pending foreign patent applications in a number of jurisdictions, including Australia, Brazil, Canada, China, the European Union member states, Israel, India, Indonesia, Japan, South Korea, Mexico, New Zealand, Russia, Singapore, South Africa, and Taiwan; four pending PCT applications; and two pending U.S. provisional patent applications directed to our Potentiator Platform. Issued U.S. or foreign patents and any patents issuing any pending U.S., foreign or PCT applications covering SPR741 will have a statutory expiration date of August 2027, February 2029, April 2037, May 2037, May 2038 and July 2038. 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, 2017, we owned one U.S. patent, three pending U.S. applications, five foreign patents and 41 pending foreign patent applications in a number of jurisdictions including Argentina, Australia, Brazil, Canada, China, Colombia, Eurasia, the European Union, Hong Kong, Israel, Indonesia, Japan, South Korea, Mexico, Russia, Singapore, South Africa, Taiwan and Vietnam. Issued U.S. or foreign patents and any patents issuing any pending U.S., foreign or PCT applications covering our next-generation polymyxin program will have a statutory expiration date of November 2032, May 2034, March 2035 and November 2035. Patent term adjustments or patent term extensions could result in later expiration dates.

Orphan NTM Infection 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, 2017, we owned ten issued U.S. patents, one pending U.S. patent application, 62 issued foreign patents, and 27 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, 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, SPR994, 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 SPR994 as an oral antibiotic for use as a monotherapy for the treatment of resistant and MDR infections. If approved, SPR994 would compete with several antibiotics currently in clinical development, including C-Scape from Achaogen, Inc., sulopenem from Iterum Therapeutics Limited, eravacycline from Tetraphase Pharmaceuticals, Inc. and omadacycline from Paratek Pharmaceuticals, Inc.

We also expect that SPR994, if approved, would compete with future and current generic versions of marketed antibiotics.

If approved, we believe that SPR994 would compete effectively against these compounds on the basis of SPR994'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;
- 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 our Potentiator Platform, SPR741 and SPR206, as IV-administered agents for Gram-negative infections in the hospital. If approved, SPR741 or our single-agent candidate SPR206 would compete with several IV-administered product candidates marketed for the treatment of Gram-negative infections, including Avycaz from Allergan plc and Pfizer Inc. and Zerbaxa from Merck & Co. There are also a number of IV-administered product candidates in late-stage clinical development that are intended to treat Gram-negative infections, including plazomicin from Achaogen Inc., meropenem-vaborbactam from The Medicines Company, cefiderocol from Shionogi & Co. Ltd., eravacycline IV from Tetraphase Pharmaceuticals Inc. and relabactam 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 as the first approved oral treatment for NTM infection. There are currently no approved agents to treat NTM infection. Current SOC is a combination of generically available options. There is one drug in late-stage development, Arikayce from Insmed. It is an inhaled version of a commonly used drug in the hospital setting called amikacin. If approved, it would potentially compete with SPR720. 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. To date, the FDA has not approved any drugs utilizing the limited population pathway. 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 SPR994 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 SPR994 for cUTI in November 2016 and CABP and DFI in April 2017, and expect to request QIDP designations for our other product candidates prior to submitting a marketing application for such product candidates, as appropriate.

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. This extension is in addition to any pediatric exclusivity extension awarded, and the extension will be awarded only to a drug first approved on or after the date of enactment.

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.

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 SPR994'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, 2017, we had 35 full-time employees, including a total of 12 employees with M.D. or Ph.D. degrees. 22 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. In addition, we have previously filed registration statements and other documents with the SEC. Any document we file may be inspected, without charge, at the SEC's public reference room at 100 F Street NE, Washington, DC 20549, or at the SEC's internet address at www.sec.gov. These website addresses are not intended to function as hyperlinks, and the information contained in our website and in the SEC's website is not intended to be a part of this filing. Information related to the operation of the SEC's public reference room may be obtained by calling the SEC at 800-SEC-0330.

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 100-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 incurred net losses in each year since our inception and anticipate that we will continue to incur significant losses for the foreseeable future, and if we are unable to achieve and sustain profitability, the market value of our common stock will likely decline.

We are a clinical-stage biopharmaceutical company with a limited operating history. We have not generated any revenue from the sale of products and have incurred losses in each year since our inception in 2013. Our net loss was $39.9 million and $32.6 million for the years ended December 31, 2017 and 2016, 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. We have financed our operations primarily through private placements of our preferred stock, collaborations and government funding for research and development. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical and clinical development.

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, as well as to support our transition to a public reporting company; 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 planned clinical trials and other studies of SPR994, seek marketing approval for SPR994 if clinical trials are successful, and evaluate the advancement of our other product candidates, including SPR741, SPR206 and SPR720. If we obtain marketing approval for SPR994 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 and cash equivalents as of December 31, 2017 will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2019. 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 and costs of our ongoing and planned clinical trials of SPR994;
- the timing and costs of our ongoing clinical trials of SPR741;
- the initiation, progress, timing, costs and results of preclinical studies and clinical trials of our other product candidates and potential product candidates;
- the amount of funding that we receive under government awards 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 SPR994 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 SPR994;
- 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, 2017, our non-dilutive sources of funding consisted of awards from CARB-X and the DoD that provide partial funding for the development of our Potentiator Platform product candidates, including SPR741, and an award from NIAID, for our SPR720 program. 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 NIAID 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 will have a period of performance from March 1, 2018 through February 28, 2019. 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 and CARB-X awards are subject to termination for convenience at any time by NIAID and CARB-X. Neither organization is obligated to provide funding to Spero beyond the base period amounts from Congressionally approved annual appropriations.

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 or 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.

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 independent registered public accounting firm has included in its report on our audited consolidated financial statements for the fiscal year ended December 31, 2016 an explanatory paragraph relating to our ability to continue as a going concern.

The report from our independent registered public accounting firm for the year ended December 31, 2016 includes an explanatory paragraph stating that our recurring losses from operations since inception and required additional funding to finance our operations raise substantial doubt about our ability to continue as a going concern. If we are unable to obtain sufficient funding, our

business, prospects, financial condition and results of operations will be materially and adversely affected and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited financial statements, and it is likely that investors will lose all or a part of their investment. Future reports from our independent registered public accounting firm may also contain statements expressing substantial doubt about our ability to continue as a going concern. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding to us on commercially reasonable terms or at all.

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

As of December 31, 2017, we had U.S. federal, state and foreign net operating loss carryforwards, or NOLs, of $76.4 million, $76.0 million and $4.3 million, respectively. Our NOLs begin to expire in 2033. 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.

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 SPR994 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 will need to transition from a development-focused company to a company with commercial activities, and we may experience difficulties in managing this transition, which could disrupt our operations.

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 SPR994, which is still under development, and our ability to develop, obtain marketing approval for and successfully commercialize SPR994. If we are unable to develop, obtain marketing approval for and successfully commercialize SPR994, 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 SPR994 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 SPR994. The success of SPR994 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;
- 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 SPR994;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales of SPR994, if approved, whether alone or in collaboration with others;
- acceptance of SPR994, if approved, by patients, the medical community and third-party payors;
- competition with other therapies; and
- a continued acceptable safety profile of SPR994 following approval.

Successful development of SPR994 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 SPR994, or if we experience delays as a result of any of these factors or otherwise, our business could be materially harmed.

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 SPR994 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 SPR994 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 SPR994 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 SPR994 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 SPR994 is a new formulation of the active pharmaceutical ingredient tebipenem that exhibited a favorable safety and efficacy profile during Phase 2 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 Phase 2, Phase 3 or other 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 SPR994 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 not 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 a trial;
- 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;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- 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 agreement 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 SPR994 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 SPR994 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 SPR994 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 SPR994 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 patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the eligibility criteria for participation in the clinical trial;
- the design of the clinical trial;

- our ability to recruit clinical trial investigators with appropriate 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 contemplated Phase 3 clinical trials of SPR994 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 SPR994 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.

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 SPR994 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.

Our clinical program for SPR994 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 planned pivotal Phase 3 clinical trial of SPR994 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 SPR994 in patients with cUTI, who will be the subjects of the clinical trial, and we have no direct clinical evidence that SPR994 is effective in treating cUTIs in humans. Although we believe that SPR994 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 SPR994 will demonstrate the expected efficacy in our planned 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 SPR994 studies will be validated in our planned 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 SPR994, or slow down or halt our product development for SPR994.

To support our accelerated clinical development strategy for SPR994, 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 SPR994 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 Global Pharma 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.
- The primary endpoint was not a composite of both clinical and microbiological outcomes.

If the FDA were to discount significantly the value of these clinical data as support for our clinical plan to proceed from a Phase 1 dose-selection clinical trial directly to a pivotal Phase 3 clinical trial of SPR994, then our clinical pathway for SPR994 could be materially delayed and we could incur material costs associated with conducting additional clinical trials.

A Phase 2 clinical trial of SPR741 would be subject to a number of specific risks that may affect the outcome of the trials, including the need to co-administer SPR741 with a companion antibiotic and identifying available development funding.

A Phase 2 clinical trial of SPR741 would be 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 SPR741 in patients with cUTI, who would be the subjects of any such clinical trial, and we have no direct clinical evidence that SPR741 as a potentiator in combination with a partner antibiotic has the potential to treat cUTI in humans. Although we believe that SPR741 as a potentiator in combination with a partner antibiotic has the potential to treat cUTI in humans based upon our nonclinical *in vitro* and *in vivo* animal model study results, these results are not necessarily predictive of the results in humans. We cannot guarantee that SPR741 as a potentiator in combination with a partner antibiotic will demonstrate the efficacy we expect to observe in patients in a Phase 2 clinical trial of SPR741. We also cannot guarantee that the projections made from the pharmacokinetic and pharmacodynamic models that we developed from our nonclinical and clinical SPR741 studies would be validated in a Phase 2 clinical trial.

In addition, we may face competition in enrolling suitable patients in any such trial 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 any such trial may result in increased development costs for SPR741, or slow down or halt our product development and approval process for SPR741.

Serious adverse events or undesirable side effects or other unexpected properties of SPR994 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 SPR994 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 SPR994, tebipenem, is approved in Japan, our formulation of tebipenem, SPR994, has not yet been tested extensively 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 SPR994 have experienced drug-related side effects including diarrhea, temporary increases in hepatic enzymes, allergic reactions, rash, and convulsions. To date, SPR741 has generally been well tolerated in clinical trials conducted in healthy subjects and there have been no reports of serious adverse events related to SPR741, but additional adverse events may emerge in any subsequent clinical trials.

If unexpected adverse events occur in any of our 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 SPR994 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, SPR994 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 the approval of such product;
- we may 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 or impose distribution or use restrictions;
- regulatory authorities may require one or more post-market studies;
- regulatory authorities may require the addition of a “black box” warning;
- we may be required to implement a 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;
- our product may become less competitive; and
- our reputation may suffer.

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

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 SPR994 or any other product candidate commercially, the product candidate may not achieve market acceptance among physicians, patients, hospitals (including pharmacy directors) and third-party payors and, ultimately, may not be commercially successful. 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. 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;
- 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 SPR994 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 SPR994 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 SPR994 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 SPR994 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 SPR994 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 of multi-drug resistant infections that we would expect would compete with SPR994, 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. If SPR994 is approved, the pricing may be at a significant premium over other competitive products. This may make it difficult for SPR994 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 C-Scape from Achaogen, Inc., sulopenem from Iterum Therapeutics Limited, eravacycline from Tetraphase Pharmaceuticals, Inc. 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 Avycaz from Allergan plc and Pfizer Inc. and Zerbaxa from Merck & Co. 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 plazomicin from Achaogen, Inc., meropenem vaborbactam from The Medicines Company, cefiderocol from Shionogi & Co. Ltd., eravacycline IV from Tetraphase Pharmaceuticals, Inc. and relabactam 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 SPR994 and our other product candidates.

Even if we are able to commercialize SPR994 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 SPR994 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 SPR994 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 SPR994 or our other product candidates, which could affect their revenue potential.

We are developing SPR994 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 SPR994 or any of such other product candidates may develop.

Specifically, neither SPR994 nor SPR741 (as a potentiator in combination with a partner antibiotic) are highly active against infections caused by *Pseudomonas aeruginosa*. As with some commercially available carbapenems, SPR994 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 SPR994 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 SPR994 or any of our other product candidates outside of controlled hospital settings, could contribute to the rise of resistance. If resistance to SPR994 or any of our other product candidates becomes prevalent, our ability to generate revenue from SPR994 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 planned clinical trials and potential approval of our lead product candidate, SPR994, our lead Potentiator Platform product candidates, SPR741 and SPR206, and SPR 720, 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. Other than SPR994 and SPR741, all of our potential product candidates remain in the discovery and preclinical stages.

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 SPR994 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 SPR994 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.

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, it could result in a material disruption of our programs. 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.

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 SPR994 ourselves in the United States, we intend to commercialize both product candidates outside the United States through collaboration arrangements. If we develop SPR741 to be co-administered in combination with branded and not generic antibiotic compounds, then we will be required to obtain and maintain rights from third-party collaborators for the development and commercialization of SPR741 co-administered with such other branded antibiotic compounds. In addition, we may seek third-party collaborators for development and commercialization of certain of our product candidates. Our

likely collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangements.

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 SPR994 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. For SPR741, if we develop such product candidate to be co-administered in combination with branded and not generic antibiotic compounds, we will be required to obtain and maintain rights from third-party collaborators for such development and commercialization of SPR741 co-administered with such collaborator's branded antibiotic compound. Moreover, we intend to utilize a variety of types of collaboration arrangements for the potential commercialization of our product candidates outside the United States.

We face significant competition in seeking and obtaining appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include:

- the design or results of clinical trials;
- the likelihood of approval by the FDA 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 some 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 good laboratory practice 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 SPR994 and SPR741 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.

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. 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 GCPs, 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 GCPs. 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 SPR994 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 SPR994 and SPR741 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 SPR994 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 SPR994 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. If our manufacturers cannot successfully manufacture material that conforms to the strict regulatory requirements of the FDA and any applicable foreign regulatory authority,

they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need 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 SPR994 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 SPR994, we could lose such rights that are important to our business.

We are a party to agreements with Meiji for SPR994, Northern for SPR741, 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 Spero rights outside of specified countries in Asia to develop, manufacture, and commercialize SPR994 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, Spero has the right to develop, manufacture and have manufactured SPR994 in Asia solely for the purpose of furthering development, manufacturing and commercialization of SPR994 outside of Asia. In exchange for those rights, Spero is obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop and commercialize SPR994 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.

Our reliance on government funding for certain of our programs adds uncertainty 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.

Aspects of our development programs are currently being supported, in part, with funding from CARB-X, the DoD and NIAID.

Contracts and grants awarded by the U.S. government, its agencies, and its partners, including our awards from CARB-X, the DoD and NIAID, include provisions that reflect the government's substantial rights and remedies, many of which are not typically found in commercial contracts, including powers of the government to:

- terminate agreements, in whole or in part, for any reason or no reason;
- reduce or modify the government's obligations under such agreements without the consent of the other party;
- claim rights, including intellectual property rights, in products and data developed under such agreements;
- audit contract-related costs and fees, including allocated indirect costs;
- suspend the contractor or grantee from receiving new contracts pending resolution of alleged violations of procurement laws or regulations;
- impose U.S. manufacturing requirements for products that embody inventions conceived or first reduced to practice under such agreements;

- suspend or debar the contractor or grantee from doing future business with the government;
- control and potentially prohibit the export of products;
- pursue criminal or civil remedies under the False Claims Act, False Statements Act and similar remedy provisions specific to government agreements; and
- limit the government's financial liability to amounts appropriated by the U.S. Congress on a fiscal-year basis, thereby leaving some uncertainty about the future availability of funding for a program even after it has been funded for an initial period.

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

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

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

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

As a U.S. government contractor, we are subject to financial audits and other reviews by the U.S. government of our costs and performance on their contracts, as well as our accounting and general business practices related to these contracts. Based on the results of its audits, the government may adjust our contract-related costs and fees, including allocated indirect costs. Although adjustments arising from government audits and reviews have not had a material adverse effect on our financial condition or results of operations in the past, we cannot make assurances that future audits and reviews will not have those effects.

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 SPR994, 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 SPR994 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 have misappropriated the intellectual property of a third party, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees 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 employees 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 not yet registered our trademarks. Failure to secure those registrations could adversely affect our business.

We have not yet registered our trademarks in the United States or other countries. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would, which could adversely affect our business. We have also 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 SPR994 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 SPR994 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 collaborator is 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 a Risk Evaluation and Mitigation Strategy, or 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.

We may seek fast track designation for SPR994 or one or more of our other product candidates, but we might not receive such designation, and in any case, such designation may not actually lead to a faster development or regulatory review or approval process.

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.

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 SPR994 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 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 fines, 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 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.

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 require 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.

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, or the Code. 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. Our net deferred tax assets and liabilities will be revalued at the newly enacted U.S. corporate rate, and the impact, if any, will be recognized in our tax expense in the year of enactment. We continue to examine the impact this tax reform legislation may have on our business. 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 common stock.

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, 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 customers or 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

An active trading market for our common stock may not develop.

Our shares of common stock began trading on The Nasdaq Global Select Market on November 2, 2017. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares may not be sustained, which could put downward pressure on the market price of our common stock and thereby affect the ability of stockholders to sell their shares. An inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

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 SPR994 and any other product candidate;
- results of clinical trials of SPR994 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;
- 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, development timelines or recommendations by securities analysts;
- 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.

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 commence coverage of us, the trading price of our stock would likely decrease. 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 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 IPO, 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 JOBS Act and may remain an emerging growth company for up to five years. 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, 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.

We will 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 will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, 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 will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors.

We are currently evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of an Annual Report on Form 10-K with the SEC after we become a public company. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

A significant portion of our total outstanding shares is restricted from immediate resale but 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. As of March 1, 2018, we had 14,369,182 shares of common stock outstanding. This includes the 5,971,498 shares that we sold in our initial public offering. The remaining 8,397,684 shares are currently restricted under securities laws or as a result of lock-up agreements. These restrictions are due to expire April 30, 2018, resulting in these shares becoming eligible for public sale on May 1, 2018, subject to applicable securities laws. Holders of an aggregate of 8,144,366 shares of our common stock will 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 filed a registration statement on Form S-8 under the Securities Act on December 14, 2017, to register all of the shares of our common stock subject to outstanding options and all shares of our common stock otherwise issuable pursuant to our equity compensation plan. As of March 1, 2018, we had options to purchase an aggregate of 2,114,782 shares of our common stock outstanding. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described above.

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 March 1, 2018, 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 53% 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 7,800 square feet of office space. In January 2018, we entered into an amendment to our Cambridge, Massachusetts facility lease. Pursuant to the amendment, we leased an additional approximately 7,800 square feet of office space in the same building. The term for the new office space is seven years from the delivery of the expansion premises to us, which we estimate to be December 1, 2018. In addition, the term of our existing office space lease has been extended so that it is coterminous with the new office space lease. We also sublease approximately 7,000 square feet of laboratory space in Watertown, Massachusetts. Our sublease extends through November 2019. 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. The following table sets forth the high and low sales prices of our common stock as reported on the Nasdaq Global Select Market for the quarter ended December 31, 2017:

	High	Low
Year Ended December 31, 2017		
Fourth quarter ended December 31, 2017	$ 15.40	$ 9.84

Holders of Record

On March 26, 2018, we had approximately 24 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.

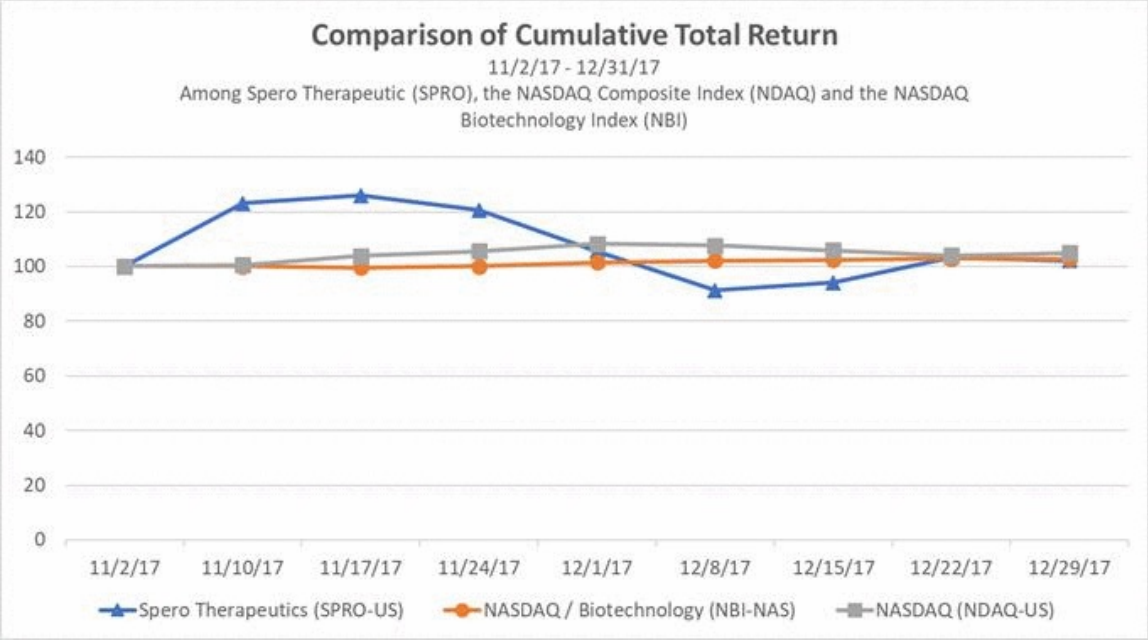
Dividends

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.

Stock Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since November 2, 2017, the date our common stock first began trading on The Nasdaq Global Select Market, to the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph assumes an initial investment of $100 in our common stock at the closing price of $11.50 on November 2, 2017 (our initial listing date), and in each of the indexes with relative performance tracked through December 31, 2017, assuming reinvestment of the full amount of all dividends, if any. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.

This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.



Recent Sales of Unregistered Securities

From January 1, 2017 through December 31, 2017, we sold and issued the following unregistered securities, which share numbers have been adjusted, as appropriate, for the one-for-6.0774 reverse stock split of our common stock that occurred on October 20, 2017:

- Prior to filing our registration statement on Form S-8 on December 14, 2017, we issued to certain of our employees, consultants and directors, options to purchase an aggregate of 2,012,106 shares of our common stock under our 2017 Stock Incentive Plan, as amended, at a weighted-average exercise price of $7.24 per share.
- On July 17, 2017, we sold 61,880 shares of our Series C preferred stock to Joel Sendek, our Chief Financial Officer, at a price of $1.7749 per share, for aggregate proceeds of $0.1 million. Upon the closing of our initial public offering on November 6, 2017, all of such shares of Series C preferred stock converted into shares of common stock, as described in Note 6 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.
- On July 17, 2017, we granted to Frank Thomas, a newly appointed member of our board of directors, stock options to purchase 30,515 shares of our common stock, at an exercise price of $5.90 per share.
- On June 30, 2017, as part of the Reorganization, each of the capital units of Spero Therapeutics, LLC issued and outstanding prior to the Reorganization was cancelled and converted into and exchanged for one share of Spero Therapeutics, Inc. capital stock of the same class and/or series as described in Note 1 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

- Prior to the Reorganization, we had granted a total of 431,375 incentive units to our employees, directors, and consultants, pursuant to the operating agreement of Spero Therapeutics, LLC, as amended, at threshold prices ranging between $1.28 and $5.84 per incentive unit. In connection with the Reorganization, such incentive units were cancelled as they were deemed to be valueless based on a liquidation valuation basis for federal income tax purposes and pursuant to contractual rights under the operating agreement of Spero Therapeutics, LLC. Promptly after the 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 on the same vesting terms and with similar rights and restrictions as the incentive units. Effective on July 6, 2017, we granted stock options to purchase an aggregate of 1,511,770 shares of our common stock. All such stock options have an exercise price of $5.90.
- In March 2017, we issued an aggregate of 29,647,582 Class C preferred units, consisting of (i) 5,321,112 Class C preferred units in exchange for 8,500 bridge units and (ii) 24,326,470 Class C preferred units at a price per unit of $1.7749 for an aggregate purchase price of approximately $43,177,052.

No underwriters were used in the foregoing transactions, and no discounts or commissions were paid. All sales of securities described above were exempt from the registration requirements of the Securities Act in reliance on Section 4(a)(2) of the Securities Act, Rule 701 promulgated under the Securities Act or Regulation D promulgated under the Securities Act, relating to transactions by an issuer not involving a public offering. All of the foregoing securities are deemed restricted securities for purposes of the Securities Act.

With respect to the foregoing transactions, the common units and incentive units, along with associated threshold prices, of Spero Therapeutics, LLC have been presented as if the one-for-6.0774 reverse stock split of our common stock that occurred on October 20, 2017 had been applied to such units and prices.

Use of Proceeds from Registered Securities

On November 6, 2017, we completed the initial public offering, or IPO, of our common stock. The offer and sale of all of the shares of our common stock in our IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-220858), which was declared effective by the SEC on November 1, 2017.

As of December 31, 2017, we had used approximately $7.4 million from the net proceeds from our IPO.

Purchases of Equity Securities by the Issuer

None.

Item 6. Selected Financial Data.

The following table sets forth selected consolidated financial data as of and for the years ended December 31, 2017, 2016 and 2015. We have derived the consolidated statement of operations data for the years ended December 31, 2017, 2016 and 2015 and the consolidated balance sheet data as of December 31, 2017 and 2016 from our audited consolidated financial statements included in this Annual Report on Form 10-K. We have derived the consolidated balance sheet data as of December 31, 2015 from our audited financial statements, which are not included in this Annual Report on Form 10-K. This information should be read in conjunction with the consolidated financial statements and the related notes thereto included in Part II, Item 8 of this Annual Report on Form 10-K and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in Part II, Item 7 of this Annual Report on Form 10-K.

	Year Ended December 31,		
	2017	2016	2015
	(In thousands, except share and per share data)		
Consolidated Statement of Operations Data:			
Grant revenue	$ 1,979	$ 335	$ —
Operating expenses:			
Research and development	32,869	26,333	11,125
General and administrative	10,840	7,223	2,202
Total operating expenses	43,709	33,556	13,327
Loss from operations	(41,730)	(33,221)	(13,327)
Other income (expense):			
Change in fair value of derivative liabilities	1,541	580	174
Interest income and other income (expense), net	303	—	—
Total other income (expense), net	1,844	580	174
Net loss	(39,886)	(32,641)	(13,153)
Less: Net loss attributable to non-controlling interest	(1,143)	(7,150)	(2,999)
Net loss attributable to Spero Therapeutics, Inc.	(38,743)	(25,491)	(10,154)
Accrued return on preferred shares	(6,146)	(3,441)	(932)
Accretion of redeemable bridge units and redeemable convertible preferred shares to redemption value	(1,208)	(996)	(2,341)
Net loss attributable to common stockholders of Spero Therapeutics, Inc.	$ (46,097)	$ (29,928)	$ (13,427)
Net loss per share attributable to common stockholders of Spero Therapeutics, Inc. per share, basic and diluted(1)	$ (17.82)	$ (95.87)	$ (53.11)
Weighted average shares outstanding, basic and diluted(1):	2,586,865	312,169	252,807

	As of December 31,		
	2017	2016	2015
	(in thousands)		
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$ 87,288	$ 10,315	$ 5,691
Working capital (deficit)	83,902	4,954	(433)
Total assets	93,479	13,772	7,176
Bridge units	—	7,924	—
Redeemable convertible preferred units	—	47,685	18,296
Total stockholders' equity (deficit)	84,957	(49,248)	(18,553)

(1) See Note 15 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for further details on the calculation of basic and diluted net loss per share attributable to common stockholders of Spero Therapeutics, Inc.

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 novel treatments for multi-drug resistant bacterial infections. Our most advanced product candidate, SPR994, 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. We also have a platform technology known as our Potentiator Platform that we believe will enable us to develop drugs that will expand the spectrum and potency of existing antibiotics, including formerly inactive antibiotics, against Gram-negative bacteria. Our lead product candidates generated from our Potentiator Platform are two intravenous, or IV,-administered agents, SPR741 and SPR206, designed to treat MDR Gram-negative infections in the hospital setting. In addition, we are developing SPR720, an oral antibiotic designed for the treatment of pulmonary non-tuberculous mycobacterial infections. 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.

On November 6, 2017, we completed an initial public offering, or IPO, of our common stock, and issued and sold 5,500,000 shares of common stock at a public offering price of $14.00 per share, resulting in net proceeds of $71.6 million after deducting underwriting discounts and commissions but before deducting offering costs. On November 14, 2017, we issued and sold an additional 471,498 shares of our common stock at the IPO price of $14.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional shares of common stock, resulting in additional net proceeds of $6.1 million after deducting underwriting discounts. Aggregate net proceeds from the IPO totaled $74.2 million after deducting underwriting discounts, commissions and offering costs.

Prior to the IPO, we funded our operations with proceeds from the sale of preferred units and bridge units and payments received under a concluded collaboration agreement and funding from government contracts. 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, 2017, we had an accumulated deficit of $96.8 million. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years.

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 operating 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.

As of December 31, 2017, we had cash and cash equivalents of $87.3 million. We believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2019.

The Reorganization

On June 30, 2017, we completed a series of transactions pursuant to which Spero Therapeutics, LLC merged with and into Spero Therapeutics, Inc., a Delaware corporation (formerly known as Spero OpCo, Inc.), with Spero Therapeutics, Inc. continuing as the surviving corporation. As part of the transactions, each issued and outstanding preferred and common unit of Spero Therapeutics, LLC outstanding immediately prior to the Reorganization was converted into and exchanged for shares of Spero Therapeutics, Inc. capital stock of the same class and/or series on a one-for-one basis, and previously outstanding incentive units of Spero Therapeutics, LLC were cancelled. In July 2017, previous holders of the cancelled incentive units who were still employed by us at the time of the Reorganization received stock options under our 2017 Stock Incentive 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 on the same vesting terms as the incentive units. All such stock options have an exercise price of $5.90 per share.

Upon consummation of the Reorganization, the historical consolidated financial statements of Spero Therapeutics, LLC became the historical consolidated financial statements of Spero Therapeutics, Inc.

Recent Developments

Initiation of Phase 1 Clinical Trial of SPR994 in Australia

In October 2017, we initiated our Phase 1 clinical trial of SPR994 in Australia. SPR994 is our novel antibiotic with potential to be the first broad-spectrum oral carbapenem approved for use in adults. While SPR994 has demonstrated a broad spectrum of activity against MDR Gram-negative bacteria, the clinical trial will focus on the treatment of complicated urinary tract infections, or cUTI. The trial is designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study to assess the safety, tolerability, food effect and pharmacokinetics of SPR994 in healthy subjects. We expect to report top-line data from this trial in mid-2018. Thereafter, we plan to request a pre-Phase 3 meeting with the Food and Drug Administration, or FDA, to confirm that no additional clinical trials or preclinical studies are required prior to initiating a Phase 3 clinical trial. Subject to feedback from the FDA, we plan to submit an investigational new drug application, or IND, and to obtain agreement on the clinical trial protocol in late 2018 and expect to initiate the pivotal Phase 3 clinical trial of SPR994 for the treatment of cUTI around year-end 2018 in support of a new drug application, or NDA.

Initiation of Phase 1b Clinical Trial of Potentiator SPR741 in the United Kingdom

In late November 2017, as described below, we initiated our Phase 1b drug-drug interaction clinical trial of SPR741 in the United Kingdom. SPR741 is one of our lead product candidates generated from our Potentiator Platform, such candidates currently consisting of SPR741 and SPR206, which are IV-administered agents designed to treat MDR Gram-negative infections in the hospital setting. SPR741 is our co-administered product candidate designed to expand the spectrum and increase the potency of a partner antibiotic when administered in combination, and SPR206 is designed to have an antibiotic activity as a single agent. In preclinical studies, SPR741 has shown an ability to potentiate over two dozen existing antibiotics and enable activity against Gram-negative pathogens.

The Phase 1b trial enrolled 27 healthy volunteers to evaluate SPR741 as a single dose in combination with compounds from the beta-lactam class of antibiotics, including cephalosporins (such as ceftazidime), monobactams (such as aztreonam) and beta-lactams/beta-lactamase inhibitors (such as piperacillin/tazobactum). The trial was designed to assess the impact, if any, on the standalone pharmacokinetics of SPR741 or the standalone pharmacokinetics of the beta-lactam combination drug when the two are dosed together as a single dose. We anticipate top-line data from this Phase 1b trial during the second quarter of 2018.

In addition, we continue to progress the development of our direct-acting Potentiator Platform molecules, exemplified by our product candidate SPR206. SPR206 is designed to also have antibiotic activity as a single agent against MDR and extremely drug resistant, or XDR, bacterial strains, including variants isolated in *Pseudomonas aeruginosa, Acinetobacter baumannii* and carbapenem-resistant *Enterobacteriaceae*.

After we receive results from the Phase 1b clinical trial of SPR741 and our ongoing preclinical toxicology study of SPR206, we intend to prioritize our product candidates for further clinical development. Our decision will be based on which program we believe represents the best opportunity for us within an optimal timeframe, factoring in the choices we must make to prioritize the opportunities within our portfolio and to best deploy our capital resources. Accordingly, for the balance of 2018, our internal

operational plans and budget and our estimate of our cash runway being sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2019 are based on us funding the development of SPR994 and SPR720 and either SPR206 or SPR741 during that period. We may seek partnering opportunities or other non-dilutive funding for further clinical development of the Potentiator candidate we elect to deprioritize.

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, all 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 may enter into in the future.

U.S. Department of Defense

In September 2016, we were awarded a cooperative agreement with the U.S. Department of Defense to further develop anti-infective agents to combat Gram-negative bacteria. The agreement is structured as a single, two-year $1.5 million award. We are eligible for the full funding from 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 partner antibiotics. We receive funding under the DoD award as we incur qualifying expenses.

NIAID

In February 2017, we received an award from the U.S. National Institute of Allergy and Infectious Diseases to conduct additional preclinical studies of SPR720. The award is structured as a 12-month $0.6 million base period, which has already been committed, and a $0.4 million option period. In February 2018 NIAID exercised the $0.4 million 12-month option period. We receive funding under the NIAID award as we incur qualifying expenses.

In June 2016, we entered into agreements with Pro Bono Bio PLC, a corporation organized under the laws of England, and certain of its affiliates, including PBB Distributions Limited and Cantab Anti-Infectives Limited, 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 CAI-held NIAID contract to us. The NIAID contract provides for development funding of up to $5.7 million over a base period and three option periods. As of December 31, 2017, funding for the base period and the first two option periods totaling $5.1 million have been committed. Novation of the NIAID contract was finalized in December 2017. We will pay PBB a percentage of funds received from NIAID up to a maximum of $1.3 million.

CARB-X

In April 2017, we received an award from the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, a public-private partnership funded by the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services, to be used to screen, identify and complete Phase 1 clinical trials with at least one partner compound for SPR741, one of our lead potentiator product candidates. The award committed 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. We receive funding from CARB-X as we incur qualifying expenses.

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;
- 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.

In April 2014, we entered into a research and development services and support agreement and an option agreement with Hoffmann-La Roche, Inc. and certain of its affiliates, or Roche, whereby we were required to use our best efforts to research and develop a specified asset while Roche would provide partial funding as well as participate in a joint steering committee for the development of this asset. The nonrefundable payments we received in 2014 and 2015 from Roche were recognized as reductions to research and development expense. We terminated our agreement with Roche in August 2016.

Prior to novation of the NIAID contract to us, 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, 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 for our SPR741 program 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.

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. The table below summarizes our research and development expenses incurred by development program:

	Year Ended December 31,		
	2017	2016	$ Change
	(in thousands)		
Direct research and development expenses by program:			
SPR994	$ 9,803	$ 989	$ 8,814
SPR741	10,381	11,728	(1,347)
SPR720	1,585	1,181	404
SPR206	1,437	—	1,437
Preclinical programs	1,337	6,510	(5,173)
Unallocated expenses:			
Personnel related (including share-based compensation)	5,724	3,633	2,091
Facility related and other	2,602	2,292	310
Total research and development expenses	$ 32,869	$ 26,333	$ 6,536

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 planned clinical and preclinical development activities in the near term and in the future as we initiate additional clinical trials and other studies of SPR994 and our other product candidates, continue to discover and develop additional product candidates, hire additional clinical, scientific and commercial 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 SPR994;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales of SPR994 and our other product candidates, if approved, whether alone or in collaboration with others;
- acceptance of SPR994 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 SPR994 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 activities and development of our product candidates. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance, and director and officer insurance costs as well as investor and public relations expenses associated with operating as a public company.

Other Income (Expense)

Change in Fair Value of Derivative Liabilities

Tranche Rights. Our Class A preferred units and Class B preferred units provided our investors with the right to participate in subsequent offerings of Class A and Class B preferred units in the event that specified milestones were achieved, which we refer to as tranche rights. We classified the tranche 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 associated with the tranche rights as a component of other income (expense) in our consolidated statement of operations and comprehensive loss. The tranche rights were settled in 2016.

Contingent Prepayment Options. Bridge units issued to our investors in 2016 were automatically convertible into equity units sold in a subsequent round of qualified financing at a discounted rate. We refer to these automatic conversion features as contingent prepayment options. We classified the contingent prepayment options as a derivative liability 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 liability associated with the contingent prepayment options as a component of other income (expense) in our consolidated statement of operations and comprehensive loss. The contingent prepayment options were settled in the first quarter of 2017 upon the issuance of Class C preferred units.

Anti-Dilution Rights. In connection with the issuance of non-controlling interests in certain of our subsidiaries, specifically Spero Potentiator, Inc., Spero Europe, Ltd. and 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. As of December 31, 2016, anti-dilution rights related to Spero Potentiator, Inc. were fully settled as the maximum number of shares to be issued to the minority investor had been reached in August 2016. 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.

As of December 31, 2017, the derivative liability of $0.2 million recorded on our consolidated balance sheet relates only to the anti-dilution rights held by the minority investor in Spero Gyrase, Inc.

Interest Income and Other Income (Expense), Net

Interest income consists of interest earned on our cash equivalents, which are invested in money market accounts. Our interest income has not been significant due to nominal investment balances and low interest earned on those balances. Other income (expense), net, consists of insignificant amounts of miscellaneous income and expenses unrelated to our core operations.

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, 2017, we had federal and state net operating loss carryforwards of $76.4 million and $76.0 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2033. In addition, as of December 31, 2017, we had foreign net operating loss carryforwards of $4.3 million, which may be available to offset future income tax liabilities and do not expire. As of December 31, 2017, we also had federal and state research and development tax credit carryforwards of $1.7 million and $0.4 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.

Prior to the Reorganization, our 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., whose consolidated financial statements are presented in this Annual Report on Form 10-K, 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.

Net Income (Loss) Attributable to Non-Controlling Interests

Net income (loss) attributable to non-controlling interests in our consolidated statement of operations and comprehensive loss is a result of minority investments in our subsidiaries, Spero Europe, Ltd., Spero Potentiator, Inc., Spero Cantab, Inc. and Spero Gyrase, Inc., and consists of the portion of the net income or loss of these subsidiaries that is not allocated to us. Changes in the amount of net income (loss) attributable to non-controlling interests are directly impacted by changes in the net income or loss of our consolidated subsidiaries and by the ownership percentage of the minority investors.

In May 2017, we repurchased 100% of the issued and outstanding shares of Spero Europe, Ltd. held by the minority investor. In June 2017, we repurchased 100% of the issued and outstanding shares of Spero Potentiator, Inc. held by the minority investor. In July 2017, we repurchased 100% of the issued and outstanding shares of Spero Cantab, Inc. held by the minority investor. As a result of these repurchases of the non-controlling interests, for periods subsequent to each repurchase, we no longer attribute net income (loss) to the non-controlling interest. As of December 31, 2017, the remaining non-controlling interest relates only to Spero Gyrase, Inc.

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. 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 have concluded to recognize funding received from the DoD, NIAID and 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. Revenue is recognized as the qualifying expenses related to the contracts are incurred. Revenue recognition commences only once persuasive evidence of a contract exists, services have been rendered, the reimbursement amounts under the contract are fixed or determinable, and collectibility is reasonably assured. Revenue recognized upon incurring qualifying expenses in advance of receipt of funding is recorded in our consolidated balance sheet as other receivables. The related costs incurred by us are included in research and development expenses 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 $1.8 million and $0.1 million during the years ended December 31, 2017 and 2016, 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 our statement of operations and comprehensive loss as a reduction of the related expense that is incurred.

For example, in 2014, we entered into a research and development services and support agreement with Roche and concluded that the agreements were not within the scope of the accounting guidance for collaboration arrangements. Due to the co-funded nature of the payments and our assessment that we did not have a vendor/customer relationship with Roche, we recognized the nonrefundable payments received under the agreement as a reduction to the research and development expenses incurred. We terminated our agreement with Roche in August 2016. Related to payments received under this concluded collaboration, we recognized reductions of research and development expense of $0.9 million and $1.5 million during the years ended December 31, 2016 and 2015, respectively.

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

Prior to the Reorganization, our former parent company, Spero Therapeutics, LLC, had granted incentive units, which we accounted for as equity-classified awards. Subsequent to the Reorganization on June 30, 2017, we began granting common stock options.

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.

For share-based awards granted to non-employee consultants, we recognize compensation expense over the period during which services are rendered by such consultants until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of our common stock or common units and updated assumption inputs in the Black-Scholes option-pricing model.

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.

Determination of the Fair Value of Common Units and Common Stock

As there was no public market for our common units and common stock prior to our IPO, the estimated fair value of our common units and common stock was determined by our board of directors as of the date of each award grant, with input from management, considering our most recently available third-party valuations and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Our common unit and common stock valuations were prepared using the option pricing method, or OPM,

which used a market approach to estimate our enterprise value. The OPM treats the company's securities as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock and, prior to the Reorganization, the common units, have value only if the funds available for distribution to stockholders exceeded the value of the preferred share liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger. A discount for lack of marketability of the common units or common stock is then applied to arrive at an indication of value for the common units or common stock. These third-party valuations were performed at various dates, which resulted in valuations of our common units of $4.08 per unit as of February 26, 2016 and $1.95 per unit as of March 10, 2017, and a valuation of our common stock of $5.90 per share as of June 30, 2017. In addition to considering the results of these third-party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our common units and common stock as of each grant date, which may be a date later than the most recent third-party valuation date, including:

- the prices at which we sold preferred units and the superior rights and preferences of the preferred stock and preferred units relative to our common stock and common units at the time of each grant;
- the progress of our research and development programs, including the status of preclinical studies and clinical trials for our product candidates;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the biotechnology industry, and trends within the biotechnology industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common and preferred stock and our common units and preferred units;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or a sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

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

Valuation of Derivative Liabilities

Tranche Rights

Our Class A preferred units and Class B preferred units provided our investors with tranche rights, which provided these investors the right to participate in subsequent offerings of Class A and Class B preferred units in the event certain milestones were achieved. We classified each of the tranche rights as a derivative liability on our consolidated balance sheet because they met the definition of freestanding financial instruments that may require us to transfer assets upon exercise. We remeasured to fair value of the derivative liabilities associated with the tranche rights at each reporting date, and we recognized changes in the fair value of the derivative liabilities as a component of other income (expense) in our consolidated statement of operations and comprehensive loss. The tranche rights were settled in 2016, and we stopped recognizing changes in the fair value of the derivative liability related to the tranche rights at that time.

The fair value of these derivative liabilities was determined using the probability-weighted expected return method, or PWERM, which considered as inputs the probability and time that a milestone would be achieved, the potential fair value of our preferred stock upon the exercise of the tranche right and the risk-adjusted discount rate.

Contingent Prepayment Option

Bridge units issued to our investors in 2015 and 2016 contained contingent prepayment options, whereby such units were automatically convertible into equity units sold in a subsequent round of qualified financing at a discounted rate. We classified the contingent prepayment options as derivative liabilities on our consolidated balance sheet because the bridge units were deemed to be more akin to debt than equity and the embedded prepayment options were at a substantial discount, thus meeting the definition of derivative liabilities. We remeasured the fair value of the derivative liabilities at each reporting date, and we recognized changes in the fair value of the derivative liabilities associated with the contingent prepayment options as a component of other income (expense) in our consolidated statement of operations and comprehensive loss. The contingent prepayment option associated with the bridge units issued in 2015 was settled in 2015 upon the issuance of Class A preferred units. The contingent prepayment option associated with the bridge units issued in 2016 was settled in the first quarter of 2017 upon the issuance of Class C preferred units in March 2017. In periods subsequent to the settlement of any contingent prepayment option, we no longer recognize changes in the fair value of the derivative liability related to the settled contingent prepayment option.

Anti-Dilution Rights

In connection with the issuance of non-controlling interests in certain of our subsidiaries, specifically Spero Potentiator, Inc., Spero Europe, Ltd. and Spero Gyrase, Inc., we granted anti-dilution rights to the minority investors. We classify the anti-dilution rights as derivative liabilities on our consolidated balance sheet because they are freestanding instruments that represent a conditional obligation to issue a variable number of shares. We remeasure the derivative liabilities associated with the anti-dilution rights to fair value at each reporting date, and we recognize changes in the fair value of the derivative liabilities as a component of other income (expense) in our consolidated statement of operations and comprehensive loss. As of December 31, 2016, anti-dilution rights related to Spero Potentiator, Inc. were fully settled as the maximum number of shares to be issued to the minority investor had been reached in August 2016. In May 2017, we repurchased 100% of the minority investor's outstanding shares in Spero Europe, Ltd., at which time the anti-dilution rights were settled. As of December 31, 2017, the derivative liability of $0.2 million recorded on our consolidated balance sheet relates only to the anti-dilution rights held by the minority investor in Spero Gyrase, Inc.

In periods subsequent to the settlement of any anti-dilution rights, we no longer recognize changes in the fair value of the derivative liability related to the settled anti-dilution right. The fair value of these derivative liabilities was determined using a discounted cash flow model. The most significant assumption in the discounted cash flow model impacting the fair value of the anti-dilution rights is the probability that we would fund the maximum amount of investment providing anti-dilution protection. The fair value of these derivative liabilities was determined using the PWERM, which considered as inputs the probability and time that a subsequent round of preferred stock financing would occur and the risk-adjusted discount rate.

Investment Option

Our concluded collaboration agreement provided our collaboration partner with an investment option, whereby the collaboration partner could participate in our next round of financing subsequent to April 2014 in an amount up to $2.0 million at 90.0% of the per unit price of the related financing. We classified the investment option as a derivative liability on our consolidated balance sheet because it met the definition of a freestanding financial instrument that may require us to transfer assets upon exercise. We remeasured the fair value of the derivative liability at each reporting date, and we recognized changes in the fair value of the derivative liability associated with the investment option as a component of other income (expense) in our consolidated statement of operations and comprehensive loss. The subsequent financing occurred in June 2015 and our collaboration partner elected not to exercise the investment option, which then expired. We stopped recognizing changes in the fair value of the derivative liability related to the investment option at that time.

The fair value of this derivative liability was determined using the PWERM, which considered as inputs the probability and time that a qualified round of preferred stock financing would occur and the risk-adjusted discount rate.

Results of Operations

Comparison of the Years Ended December 31, 2017 and 2016

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

	Year Ended December 31,		
	2017	2016	$ Change
	(in thousands)		
Grant revenue	$ 1,979	$ 335	$ 1,644
Operating expenses:			
Research and development	32,869	26,333	6,536
General and administrative	10,840	7,223	3,617
Total operating expenses	43,709	33,556	10,153
Loss from operations	(41,730)	(33,221)	(8,509)
Other income (expense):			
Change in fair value of derivative liabilities	1,541	580	961
Interest income and other income (expense), net	303	—	303
Total other income (expense), net	1,844	580	1,264
Net loss and comprehensive loss	(39,886)	(32,641)	(7,245)
Less: Net loss attributable to non-controlling interest	(1,143)	(7,150)	6,007
Net loss attributable to Spero Therapeutics, Inc.	$ (38,743)	$ (25,491)	$ (13,252)

Grant Revenue

Grant revenue recognized during 2017 was primarily due to the reimbursement of qualifying expenses incurred in connection with our CARB-X award related to our SPR741 program of $0.9 million as well as $0.7 million under our award from the DoD, also related to our SPR741 program. We also recognized $0.4 million under our award from NIAID related to our SPR720 program. During the year ended December 31, 2016, all recognized revenue related to the reimbursement of qualifying expenses incurred in connection with our SPR741 program under our research and development award from the DoD.

Research and Development Expenses

	Year Ended December 31,		
	2017	2016	$ Change
		(in thousands)	
Direct research and development expenses by program:			
SPR994	$ 9,803	$ 989	$ 8,814
SPR741	10,381	11,728	(1,347)
SPR720	1,585	1,181	404
SPR206	1,437	—	1,437
Preclinical programs	1,337	6,510	(5,173)
Unallocated expenses:			
Personnel related (including share-based compensation)	5,724	3,633	2,091
Facility related and other	2,602	2,292	310
Total research and development expenses	$ 32,869	$ 26,333	$ 6,536

We designated SPR994 as a product candidate in the fourth quarter of 2016. Direct costs related to our SPR994 program during 2017 were primarily due to preclinical manufacturing and preclinical costs as we focused efforts on formulation development, manufacturing process and manufacturing of clinical trial material in anticipation of a Phase 1 clinical trial, which commenced in October 2017. We also incurred $1.6 million of research and development expense related to a payment of $1.0 million to Meiji Seika Pharma Co. Ltd. that became due and was paid in October 2017 under our know-how license with Meiji upon the enrollment of the first patient in clinical trials and $0.6 million for an upfront license fee paid to Meiji.

Direct costs related to our SPR741 program decreased primarily due to a decrease in preclinical costs resulting from costs incurred in the prior year to support our CTN filing in Australia in the fourth quarter of 2016, partially offset by an increase in clinical trial costs and manufacturing costs as well as expense related to a total payment to Northern Antibiotics OY Ltd. of $2.6 million which became due and was paid under our agreements with Northern upon the completion of our IPO in November 2017. The increase in clinical trial costs and manufacturing costs was due to our Phase 1 clinical trial of SPR741, which was initiated in the fourth quarter of 2016, as well as manufacturing of clinical trial materials for our Phase 1b drug-drug interaction clinical trial of SPR741 in the United Kingdom, which was initiated in November 2017, and a possible Phase 2 clinical trial. Research and development expenses for our SPR741 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 $1.8 million in the year ended December 31, 2017.

We designated SPR720 as a product candidate in the second half of 2016. Direct costs related to our SPR720 program during the year ended December 31, 2017 were primarily due to preclinical and manufacturing costs related to IND-enabling toxicology studies.

We designated SPR206 as a product candidate in July 2017. Direct costs related to our SPR206 program during the year ended December 31, 2017 were primarily due to preclinical and manufacturing costs related to IND-enabling toxicology studies.

Direct costs related to our preclinical programs decreased by $5.2 million during the year ended December 31, 2017 compared to the prior year due primarily to the cost of in-licensing technology incurred in 2016 of $5.1 million and to decreased spending on preclinical programs in 2017. The cost of in-licensing technology incurred in 2016 of $5.1 million was a result of the issuance of equity and anti-dilution rights to Promiliad Biopharma Inc., or Promiliad, Biota Pharmaceuticals, Inc. (now Aviragen Therapeutics, Inc.), or Aviragen, and PBB, and a license fee payment of $0.5 million we made to Vertex Pharmaceuticals Inc., or Vertex. Our research and development expenses related to our preclinical programs decreased in 2017 as compared to 2016 as we focused development efforts on our product candidates. Direct costs related to our preclinical programs were recorded net of the recognition of funding received from a concluded collaboration agreement of $0.9 million during the year ended December 31, 2016.

The increase in personnel-related costs included in unallocated expenses was due to an increase in headcount in our research and development function. Personnel-related costs for the years ended December 31, 2017 and 2016 included share-based compensation

expense of $0.4 million and $0.1 million, respectively. The increase in facility-related and other costs was primarily due to new laboratory space and 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,		
	2017	2016	$ Change
	(in thousands)		
Personnel related (including share-based compensation)	$ 4,330	$ 2,243	$ 2,087
Professional and consultant fees	5,829	4,145	1,684
Facility related and other	681	835	(154)
Total general and administrative expenses	$ 10,840	$ 7,223	$ 3,617

The increase in personnel-related costs was primarily a result of an increase in headcount in our general and administrative function and an increase in stock-based compensation expense related to additional employee stock options granted at a higher fair value of our common stock. Personnel-related costs for the years ended December 31, 2017 and 2016 included share-based compensation expense of $1.1 million and $0.1 million, respectively.

The increase in professional and consultant fees primarily consisted of an increase in professional fees, including accounting, audit, business development and legal fees, as well as costs associated with ongoing business activities and our preparations to operate as a public company. We also incurred increased legal fees in connection with the Reorganization.

Other Income (Expense), Net

Other income, net was $1.8 million for the year ended December 31, 2017, compared to $0.6 million for the year ended December 31, 2016. The increase in other income was primarily due to a decrease of $1.5 million in the fair value of the derivative liability for anti-dilution rights granted to minority investors in Spero Gyrase Inc. and Spero Europe Ltd. resulting from our discontinuation of the underlying development programs of these subsidiaries. We also had interest income of $0.3 million in the twelve months ended December 31, 2017 as a result of interest earned on invested cash balances.

Comparison of the Years Ended December 31, 2016 and 2015

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015:

	Year Ended December 31,		
	2016	2015	$ Change
	(in thousands)		
Grant revenue	$ 335	$ —	$ 335
Operating expenses:			
Research and development	26,333	11,125	15,208
General and administrative	7,223	2,202	5,021
Total operating expenses	33,556	13,327	20,229
Loss from operations	(33,221)	(13,327)	(19,894)
Other income (expense):			
Change in fair value of derivative liabilities	580	174	406
Total other income (expense), net	580	174	406
Net loss and comprehensive loss	(32,641)	(13,153)	(19,488)
Less: Net loss attributable to non-controlling interest	(7,150)	(2,999)	(4,151)
Net loss attributable to Spero Therapeutics, Inc.	$ (25,491)	$ (10,154)	$ (15,337)

Grant Revenue

During the year ended December 31, 2016, all recognized grant revenue related to the reimbursement of qualifying expenses incurred in connection with our SPR741 program under our research and development award from the DoD.

Research and Development Expenses

	Year Ended December 31,		
	2016	2015	$ Change
	(in thousands)		
Direct research and development expenses by program:			
SPR994	$ 989	$ —	$ 989
SPR741	11,728	6,144	5,584
SPR720	1,181	—	1,181
SPR206 and other preclinical programs	6,510	2,479	4,031
Unallocated expenses:			
Personnel related (including share-based compensation)	3,633	1,742	1,891
Facility related and other	2,292	760	1,532
Total research and development expenses	$ 26,333	$ 11,125	$ 15,208

We designated SPR994 as a product candidate in the second half of 2016. Direct costs related to our SPR994 program during the year ended December 31, 2016 were primarily due to preclinical and manufacturing costs as we focused efforts on formulation development, manufacturing process and manufacturing of clinical trial material in anticipation of a Phase 1 clinical trial.

Direct costs related to our SPR741 program increased by $5.6 million, primarily due to an increase of $8.4 million in preclinical costs, partially offset by the cost of in-licensing technology under the program incurred in 2015 of $3.5 million. The increase in preclinical costs was primarily due to costs incurred to support our CTN filing in Australia in the fourth quarter of 2016. The cost of in-licensing technology under the SPR741 program incurred in 2015 of $3.5 million was a result of the issuance of equity and anti-dilution rights to Northern Antibiotics Oy Ltd., or Northern. Research and development expenses for our SPR741 program conducted by our Australian subsidiary were recorded net of a 43.5% research and development tax incentive from the Australian government of $0.1 million in the year ended December 31, 2016.

We designated SPR720 as a product candidate in the second half of 2016. Direct costs related to our SPR720 program during the year ended December 31, 2016 were primarily due to preclinical costs related to IND-enabling toxicology studies and other preclinical studies.

Direct costs related to our SPR206 program and other preclinical programs increased by $4.0 million primarily due to the cost of in-licensing technology of $5.1 million, partially offset by a decrease in preclinical costs as we increased our focus on our more advanced programs, including SPR994 and SPR720, which we designated as product candidates in the second half of 2016. The cost of in-licensing technology incurred in 2016 of $5.1 million was a result of the issuance of equity and anti-dilution rights to Promiliad, Aviragen and PBB and a license fee payment of $0.5 million we made to Vertex in the first half of 2016. Our preclinical programs expense was recorded net of the recognition of funding received from a concluded collaboration agreement of $1.5 million and $0.9 million in the years ended December 31, 2015 and 2016, respectively.

The increase in personnel-related costs included in unallocated expenses of $1.9 million was due to an increase in headcount in our research and development function. Personnel-related costs for the years ended December 31, 2015 and 2016 included share-based compensation expense of less than $0.1 million and $0.1 million, respectively. The increase in facility-related and other costs was primarily due to new laboratory space and 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,		
	2016	2015	$ Change
	(in thousands)		
Personnel related (including share-based compensation)	$ 2,243	$ 896	$ 1,347
Professional and consultant fees	4,145	1,109	3,036
Facility related and other	835	197	638
Total general and administrative expenses	$ 7,223	$ 2,202	$ 5,021

The increase in professional and consultant fees of $3.0 million was primarily due to increases in legal fees relating to business development, regulatory and patent costs, accounting and audit fees and public and investor relations fees due to ongoing business activities. Personnel-related costs increased by $1.3 million as a result of an increase in headcount in our general and administrative function. Personnel-related costs for the years ended December 31, 2015 and 2016 included share-based compensation expense of less than $0.1 million and $0.1 million, respectively. The increase in facility-related and other costs of $0.6 million was primarily due to the lease of office space that we entered into at the end of 2015, software costs and general support costs for the increase in headcount.

Other Income (Expense), Net

Other income, net was $0.6 million for the year ended December 31, 2016, compared to $0.2 million for the year ended December 31, 2015. The increase of $0.4 million was primarily due to a decrease of $0.6 million in the fair value of the derivative liability associated with the Class B tranche rights resulting from a decrease in the fair value of our Class B preferred units over the same period, partially offset by an increase of $0.2 million in the fair value of the derivative liability associated with the investment option held by our former collaboration partner.

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 and CARB-X. 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 a concluded collaboration agreement and funding from government contracts and, in November 2017, with proceeds from the IPO of our common stock. As of December 31, 2017, we had cash and cash equivalents of $87.3 million.

On November 6, 2017, we completed an IPO of our common stock, and issued and sold 5,500,000 shares of common stock at a public offering price of $14.00 per share, resulting in net proceeds of $71.6 million after deducting underwriting discounts and commissions but before deducting offering costs. On November 14, 2017, we issued and sold an additional 471,498 shares of our common stock at the IPO price of $14.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional shares of common stock, resulting in additional net proceeds of $6.1 million after deducting underwriting discounts and commissions. Aggregate net proceeds from the IPO totaled $74.2 million after deducting underwriting discounts, commissions and offering costs.

Cash Flows

The following table summarizes our sources and uses of cash for the years ended December 31, 2017, 2016 and 2015:

	Year Ended December 31,		
	2017	2016	2015
	(in thousands)		
Cash used in operating activities	$ (39,111)	$ (28,959)	$ (9,608)
Cash used in investing activities	(27)	(830)	(232)
Cash provided by financing activities	116,111	34,413	15,275
Net increase in cash and cash equivalents	$ 76,973	$ 4,624	$ 5,435

Operating Activities

Net cash used in operating activities for the year ended December 31, 2017 was $39.1 million, primarily resulting from our net loss of $39.9 million, adjusted for net non-cash items of $0.3 million. Net cash used by changes in our operating assets and liabilities was $0.4 million and consisted primarily of a $2.5 million increase in receivables related to the Australian research and development tax incentive and to our government contracts, partially offset by an increase in accounts payable and accrued expenses and other current liabilities of $3.7 million.

During the year ended December 31, 2016, operating activities used $29.0 million of cash, primarily resulting from our net loss of $32.6 million and cash used by changes in our operating assets and liabilities of $0.8 million, partially offset by net non-cash charges of $4.5 million. Net cash used by changes in our operating assets and liabilities for the year ended December 31, 2016 consisted primarily of a $1.0 million increase in prepaid expenses and other current assets, a $0.9 million decrease in advance payments from collaborator, a $0.6 million decrease in accounts payable, a $0.4 million increase in receivables related to our government awards and the Australian research and development tax incentive, partially offset by a $2.3 million increase in accrued expenses and other current liabilities. The decrease in advance payments from collaborator was primarily a result of the recognition of research funding received in prior periods as an offset to research and development expense as well as the termination of our collaboration agreement in August 2016, at which time we recognized the remaining portion of the liability that had been recorded in a prior year.

During the year ended December 31, 2015, operating activities used $9.6 million of cash, primarily resulting from our net loss of $13.2 million, partially offset by net non-cash charges of $3.4 million and cash provided by changes in our operating assets and liabilities of $0.2 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2015 consisted primarily of a $0.7 million increase in accounts payable and a $0.4 million increase in accrued expenses and other current

liabilities, partially offset by a decrease in advance payments from collaborator of $0.5 million as a result of the recognition of payments received in 2014 as an offset to research and development expenses, an increase in prepaid expenses and other current assets of $0.3 million and an increase in deposits of $0.2 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

We did not use any significant cash for investing activities during the year ended December 31, 2017. During the years ended December 31, 2016 and 2015, net cash used in investing activities was $0.8 million and $0.2 million, respectively, consisting of purchases of property and equipment, primarily for our new office and laboratory spaces.

Financing Activities

During the year ended December 31, 2017, net cash provided by financing activities was $116.1 million, consisting primarily of net proceeds of $74.2 million from the completion of our IPO in November 2017, as well as $43.1 million from the sale of our Class C preferred units, partially offset by $1.2 million of cash used to purchase outstanding shares of Spero Potentiator, Inc. and Spero Cantab, Inc. from the minority interest holders.

During the year ended December 31, 2016, net cash provided by financing activities was $34.4 million, consisting of net proceeds of $25.9 million from the sale of our Class B preferred units and proceeds of $8.5 million the sale of our 2016 bridge units.

During the year ended December 31, 2015, net cash provided by financing activities was $15.3 million, consisting primarily of proceeds of $8.0 million from the sale of our 2015 bridge units and net proceeds of $7.3 million from the sale of our Class A preferred units.

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 operating as a public company. The timing and amount of our operating expenditures will depend largely on:

- the timing and costs of our planned clinical trials of SPR994;
- 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 SPR994 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 SPR994;
- 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.

Based on our current plans, we believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2019. However, we do not expect that these funds will be sufficient to fund the development of our product candidates through regulatory approval and commercialization. In particular, we anticipate that these funds will not be sufficient to enable us to complete our pivotal Phase 3 clinical trial of SPR994. After we receive results from the Phase 1b clinical trial of SPR741 and our ongoing preclinical toxicology study of SPR206, we intend to prioritize our product candidates for further clinical development. Our decision will be based on which program we believe represents the best opportunity for us within an optimal timeframe, factoring in the choices we must make to prioritize the opportunities within our portfolio and to best deploy our capital resources. Accordingly, for the balance of 2018, our internal operational plans and budget and our estimate of our cash runway being sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2019 are based on us funding the development of SPR994 and SPR720 and either SPR206 or SPR741 during that period. We may seek partnering opportunities or other non-dilutive funding for further clinical development of the potentiator candidate we elect to deprioritize. 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, 2017 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)	2,127	820	1,307	—	—
Total	$ 2,127	$ 820	$ 1,307	$ —	$ —

(1) Reflects payments due for our leases of office and laboratory space under operating lease agreements that expire in 2019 and 2020.

In addition to the lease obligations above, on January 17, 2018, we entered into an amendment, or the Amendment, to our operating lease agreement for our corporate headquarters located at 675 Massachusetts Avenue, Cambridge, Massachusetts, to add approximately 7,800 square feet of office space. The Amendment also extends the expiration date of the original lease from 2020 to 2025. The Amendment requires additional annual payments of $0.5 million beginning in December 2018.

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. 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 SPR994.

Under our license agreement with Northern, we are obligated to make milestone payments of up to an aggregate of $7.0 million upon the achievement of specified clinical, commercial and other milestones. Upon the closing of our IPO in November 2017, we paid Northern $2.6 million in connection with this license agreement.

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 ($6.7 million as of December 31, 2017) 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.

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.

Under our agreement with Aviragen, we are 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 we acquired under the agreement. We are no longer pursuing development of the technology acquired under the agreement.

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.

Our cash and cash equivalents as of December 31, 2017 consisted of cash and money market accounts. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of interest rates. Because of the short-term nature of the instruments in our portfolio, a sudden change in market interest rates would not be expected to have a material impact on our financial position or results of operations.

Item 8. Financial Statements and Supplementary Data.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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 as of December 31, 2017 and 2016 and the related consolidated statements of operations and comprehensive loss, of bridge units, redeemable convertible preferred shares and stockholders' equity (deficit) and of cash flows for each of the three years in the period ended December 31, 2017, 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, 2017 and 2016, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2017 in conformity with accounting principles generally accepted in the United States of America.

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 audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

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

Emphasis of Matter

As discussed in Note 1 to the consolidated financial statements, the Company will require additional financing to fund future operations. Management's plans in regard to this matter are described in Note 1.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
April 2, 2018

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,	
	2017	2016
Assets		
Current assets:		
Cash and cash equivalents	$ 87,288	$ 10,315
Other receivables	1,011	304
Tax incentive receivables, current	1,932	—
Prepaid expenses and other current assets	1,828	1,253
Total current assets	92,059	11,872
Tax incentive receivables	—	144
Property and equipment, net	1,164	1,500
Deposits	206	206
Restricted cash	50	50
Total assets	$ 93,479	$ 13,772
Liabilities, Bridge Units, Redeemable Convertible Preferred Shares and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 3,470	$ 1,139
Accrued expenses and other current liabilities	4,321	2,928
Derivative liabilities	223	2,708
Deferred rent	143	143
Total current liabilities	8,157	6,918
Deferred rent, net of current portion	365	493
Total liabilities	8,522	7,411
Commitments and contingencies (Note 11)		
Bridge units	—	7,924
Redeemable convertible preferred units (Class A, B, C and Junior); no units authorized, issued or outstanding as of December 31, 2017; 13,549,685 units issued and outstanding as of December 31, 2016, aggregate liquidation preference of $50,326 as of December 31, 2016	—	47,685
Stockholders' equity (deficit):		
Common units, zero and 335,281 units issued and outstanding as of December 31, 2017 and 2016, respectively	—	—
Preferred stock, $0.001 par value; 10,000,000 and zero shares authorized as of December 31, 2017 and 2016, respectively	—	—
Common stock, $0.001 par value; 60,000,000 shares authorized as of December 31, 3017; 14,369,182 shares issued and outstanding as of December 31, 2017; no shares authorized, issued or outstanding as of December 31, 2016	14	—
Additional paid-in capital	181,428	—
Accumulated deficit	(96,840)	(45,440)
Total Spero Therapeutics, Inc. stockholders' equity (deficit)	84,602	(45,440)
Non-controlling interests	355	(3,808)
Total stockholders' equity (deficit)	84,957	(49,248)
Total liabilities, redeemable convertible preferred units, and stockholders' equity (deficit)	$ 93,479	$ 13,772

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,		
	2017	2016	2015
Grant revenue	$ 1,979	$ 335	$ —
Operating expenses:			
Research and development	32,869	26,333	11,125
General and administrative	10,840	7,223	2,202
Total operating expenses	43,709	33,556	13,327
Loss from operations	(41,730)	(33,221)	(13,327)
Other income (expense):			
Change in fair value of derivative liabilities	1,541	580	174
Interest income and other income (expense), net	303	—	—
Total other income (expense), net	1,844	580	174
Net loss and comprehensive loss	(39,886)	(32,641)	(13,153)
Less: Net loss attributable to non-controlling interest	(1,143)	(7,150)	(2,999)
Net loss attributable to Spero Therapeutics, Inc.	(38,743)	(25,491)	(10,154)
Cumulative dividends on redeemable convertible preferred shares	(6,146)	(3,441)	(932)
Accretion of redeemable bridge units and redeemable convertible preferred shares to redemption value	(1,208)	(996)	(2,341)
Net loss attributable to common shareholders of Spero Therapeutics, Inc.	$ (46,097)	$ (29,928)	$ (13,427)
Net loss per share attributable to common shareholders per share, basic and diluted	$ (17.82)	$ (95.87)	$ (53.11)
Weighted average shares outstanding, basic and diluted:	2,586,865	312,169	252,807

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

SPERO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF BRIDGE UNITS, REDEEMABLE CONVERTIBLE PREFERRED SHARES AND STOCKHOLDERS' EQUITY (DEFICIT)

(In thousands, except unit and share amounts)

	Bridge Units		Preferred Units		Preferred Stock		Common Units		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Spero Therapeutics, Inc. Stockholders' Equity (Deficit)	Non-controlling Interest	Total Stockholders' Equity (Deficit)
	Units	Amount	Units	Amount	Shares	Amount	Units	Par Value	Shares	Par Value					
Balances at December 31, 2014	—	$ —	3,438,318	$ 3,513	—	$ —	356,397	$ —	—	$ —	$ 65	$ (6,178)	$ (6,113)	$ —	$ (6,113)
Issuance of bridge units, net of derivative liability of $2,307	8,000	5,693	—	—	—	—	—	—	—	—	—	—	—	—	—
Deemed contribution of capital for reduction in conversion discount	—	—	—	—	—	—	—	—	—	—	1,419	—	1,419	—	1,419
Conversion of bridge units into Class A preferred units, net of tranche rights derivative liability of $1,301	(8,000)	(8,000)	2,279,202	7,587	—	—	—	—	—	—	—	—	—	—	—
Issuance of Class A preferred units, net of tranche rights of $1,100 and offering costs of $170	—	—	1,923,076	6,230	—	—	—	—	—	—	—	—	—	—	—
Cumulative dividends on redeemable convertible preferred units	—	—	—	932	—	—	—	—	—	—	(932)		(932)	—	(932)
Accretion of bridge units to redemption value	—	2,307	—	—	—	—	—	—	—	—	(539)	(1,768)	(2,307)	—	(2,307)
Accretion of preferred units to redemption value	—	—	—	34	—	—	—	—	—	—	(34)	—	(34)	—	(34)
Share-based compensation expense	—	—	—	—	—	—	—	—	—	—	21	—	21	—	21
Issuance of 49.9% non-controlling interest in Spero Potentiator in exchange for licensed technology	—	—	—	—	—	—	—	—	—	—	—	—	—	1,087	1,087
Issuance of additional shares in Spero Potentiator to minority investor under anti-dilution rights	—	—	—	—	—	—	—	—	—	—	—	—	—	1,459	1,459
Net loss	—	—	—	—	—	—	—	—	—	—	—	(10,154)	(10,154)	(2,999)	(13,153)
Balances at December 31, 2015	—	—	7,640,596	18,296	—	—	356,397	—	—	—	—	(18,100)	(18,100)	(453)	(18,553)
Deemed contribution of capital for settlement of Class A preferred unit tranche rights	—	—	—	—	—	—	—	—	—	—	2,408		2,408		2,408
Issuance of Class B preferred units, net of tranche rights derivative liability of $909 and offering costs of $112	—	—	5,909,089	24,979	—	—	—	—	—	—	—	—	—	—	—
Issuance of bridge units, net of contingent prepayment option derivative liability of $908	8,500	7,897	—	—	—	—	—	—	—	—	—	—	—	—	—
Repurchase of unvested common units	—	—	—	—	—	—	(21,116)	—	—	—	—	—	—	—	—
Cumulative dividends on redeemable convertible preferred units	—	—	—	3,441	—	—	—	—	—	—	(2,503)	(938)	(3,441)	—	(3,441)
Accretion of redeemable preferred units to redemption value	—	—	—	969	—	—	—	—	—	—	(58)	(911)	(969)	—	(969)
Accretion of bridge units to redemption value	—	27	—	—	—	—	—	—	—	—	(27)	—	(27)	—	(27)
Issuance of 20% non-controlling interest in Spero Gyrase in exchange for acquired technology	—	—	—	—	—	—	—	—	—	—	—	—	—	1,080	1,080
Issuance of 5% non-controlling interest in Spero Europe in exchange for licensed technology	—	—	—	—	—	—	—	—	—	—	—	—	—	100	100
Issuance of 12.5% non-controlling interest in Spero Cantab in exchange for licensed technology	—	—	—	—	—	—	—	—	—	—	—	—	—	1,635	1,635
Issuance of additional shares in Spero Potentiator to minority investor under anti-dilution rights	—	—	—	—	—	—	—	—	—	—	—	—	—	980	980
Share-based compensation expense	—	—	—	—	—	—			—	—	180		180	—	180
Net loss	—	—	—	—	—	—	—	—	—	—	—	(25,491)	(25,491)	(7,150)	(32,641)
Balances at December 31, 2016	8,500	7,924	13,549,685	47,685	—	—	335,281	—	—	—	—	(45,440)	(45,440)	(3,808)	(49,248)
Accretion of bridge units to redemption value	—	576	—	—	—	—	—	—	—	—	(123)	(453)	(576)	—	(576)
Conversion of bridge units into Class C preferred units	(8,500)	(8,500)	5,321,112	9,444	—	—	—	—	—	—	—	—	—	—	—
Issuance of Class C preferred units, net of issuance costs of $176	—	—	24,326,470	43,001	—	—	—	—	—	—	—	—	—	—	—
Purchase of non-controlling interest in Spero Europe			—	—	—	—	—	—	—	—	—	(14)	(14)	14	—
Purchase of non-controlling interest in Spero Potentiator			—	—	—	—	—	—	—	—	—	(7,395)	(7,395)	6,395	(1,000)
Purchase of non-controlling interest in Spero Cantab			—	—	—	—	—	—	—	—	928	—	928	(1,103)	(175)

Cumulative dividends on redeemable convertible preferred units	—	—	—	3,261	—	—	—	—	—	—	—	(3,261)	(3,261)	—	(3,261)
Accretion of redeemable preferred units to redemption value	—	—	—	369	—	—	—	—	—	—	—	(369)	(369)	—	(369)
Exchange of units in Spero Therapeutics, LLC for shares in Spero Therapeutics, Inc. on a one-for-one basis	—	—	(43,197,267)	(103,760)	43,197,267	103,760	(335,281)	—	335,281		—	—	—	—	—
Issuance of Series C preferred stock	—	—	—	—	61,880	110	—	—	—	—	—	—	—	—	—
Cumulative dividends on redeemable convertible preferred shares	—	—	—	—	—	2,885	—	—	—	—	(1,983)	(902)	(2,885)	—	(2,885)
Accretion of preferred stock to redemption value	—	—	—	—	—	263	—	—	—	—	—	(263)	(263)	—	(263)
Issuance of common stock, conversion of preferred stock to common stock	—	—	—	—	(43,259,147)	(107,018)	—	—	8,062,403	8	107,010	—	107,018	—	107,018
Issuance of common stock, initial public offering net of issuance costs of $3,574	—	—	—	—	—	—	—	—	5,971,498	6	74,169	—	74,175	—	74,175
Share-based compensation expense	—	—	—	—	—	—	—	—	—	—	1,427	—	1,427	—	1,427
Net loss	—	—	—	—	—	—	—	—	—	—	—	(38,743)	(38,743)	(1,143)	(39,886)
Balances at December 31, 2017	—	$ —	—	$ —	—	$ —	—	$ —	14,369,182	$ 14	$ 181,428	$ (96,840)	$ 84,602	$ 355	$ 84,957

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

SPERO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	2017	2016	2015
Cash flows from operating activities:			
Net loss	(39,886)	$ (32,641)	$ (13,153)
Adjustments to reconcile net loss to net cash used in operating activities:			
Non-cash research and development expense	—	4,595	3,517
Depreciation and amortization	363	279	11
Change in fair value of derivative liabilities	(1,541)	(580)	(174)
Share-based compensation	1,427	180	21
Unrealized foreign currency transaction loss	83	—	—
Changes in operating assets and liabilities:			
Other receivables	(707)	(294)	(10)
Prepaid expenses and other current assets	(575)	(966)	(280)
Tax incentive receivables	(1,811)	(144)	—
Deposits	—	(53)	(150)
Accounts payable	2,349	(644)	671
Accrued expenses and other current liabilities	1,315	2,322	409
Deferred rent	(128)	(84)	—
Advance payments from collaborator	—	(929)	(470)
Net cash used in operating activities	(39,111)	(28,959)	(9,608)
Cash flows from investing activities:			
Purchases of property and equipment	(27)	(830)	(232)
Net cash used in investing activities	(27)	(830)	(232)
Cash flows from financing activities:			
Proceeds from initial public offering of common stock, net of commissions and underwriting discounts	77,749	—	—
Payment of initial public offering costs	(3,574)	—	—
Proceeds from issuance of Class A preferred units, net of issuance costs	—	—	7,330
Proceeds from issuance of bridge units	—	8,500	8,000
Changes in restricted cash	—	—	(30)
Payment of offering costs related to 2016 issuance of Class B preferred units	—	—	(25)
Proceeds from issuance of Class B preferred units, net of issuance costs	—	25,913	—
Proceeds from issuance of Class C preferred units, net of issuance costs	43,111	—	—
Cash payment for non-controlling interests	(1,175)	—	—
Net cash provided by financing activities	116,111	34,413	15,275
Net increase in cash and cash equivalents	76,973	4,624	5,435
Cash and cash equivalents at beginning of period	10,315	5,691	256
Cash and cash equivalents at end of period	$ 87,288	$ 10,315	$ 5,691
Supplemental disclosure of non-cash investing and financing activities:			
Conversion of bridge units into preferred units	$ 8,500	$ —	$ 8,000
Conversion of preferred stock to common stock	$ 107,018	$ —	$ —
Settlement of derivative liabilities upon issuance of preferred units	$ 944	$ —	$ 888
Issuance of tranche rights with preferred units	$ —	$ 909	$ 2,401
Deemed contribution of capital	$ —	$ 2,408	$ 1,419
Settlement of derivative liability upon issuance of bridge units	$ —	$ 305	$ —
Issuance of contingent prepayment option with bridge units	$ —	$ 908	$ —
Cumulative dividends on redeemable convertible preferred shares	$ 6,146	$ 3,441	$ 932
Accretion of redeemable convertible preferred units and stock to redemption value	$ 632	$ 969	$ 34
Accretion of bridge units to redemption value	$ 576	$ 27	$ 2,307
Issuance of additional shares of common stock to minority investors under anti-dilution rights	$ —	$ 980	$ 1,459
Purchases of property and equipment included in accounts payable, accrued expenses and deferred rent	$ —	$ —	$ 728
Deferred offering costs included in accounts payable and accrued expenses	$ —	$ —	$ 11

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"), is a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing and commercializing novel treatments for multi-drug resistant ("MDR") bacterial infections. The Company's most advanced product candidate, SPR994, 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 also has a platform technology known as its Potentiator Platform that it believes will enable it to develop drugs that will expand the spectrum and potency of existing antibiotics, including formerly inactive antibiotics, against Gram-negative bacteria. The Company's lead product candidates generated from its Potentiator Platform are two intravenous, or IV,-administered agents, SPR741 and SPR206, designed to treat MDR Gram-negative infections in the hospital setting. In addition, the Company is developing SPR720, an oral antibiotic designed for the treatment of pulmonary non-tuberculous mycobacterial infections. The Company believes that its 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.

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.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Product candidates currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

On October 20, 2017, the Company effected a one-for-6.0774 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of the Company's Preferred Stock (see Note 5). Accordingly, all share and per share amounts for all periods presented in the accompanying consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the preferred stock conversion ratios. In addition, all common units and incentive units as well as the conversion ratios of preferred units of Spero Therapeutics, LLC have been presented as if the reverse stock split of the common stock of Spero Therapeutics, Inc. had been applied to such units and ratios of Spero Therapeutics, LLC.

On November 6, 2017, Spero Therapeutics, Inc. completed an initial public offering ("IPO") of its common stock, and issued and sold 5,500,000 shares of common stock at a public offering price of $14.00 per share, resulting in net proceeds of $71.6 million after deducting underwriting discounts and commissions but before deducting offering costs. On November 14, 2017, Spero Therapeutics, Inc., issued and sold an additional 471,498 shares of its common stock at the IPO price of $14.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional shares of common stock, resulting in additional net proceeds of $6.1 million after deducting underwriting discounts and commissions. Upon the closing of the IPO in November 2017, the Company's outstanding convertible preferred shares automatically converted into shares of common stock (see Note 6).

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. 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 IPO completed in November 2017. The Company has incurred recurring losses since inception, including net losses attributable to Spero Therapeutics, Inc. of $38.7 million, $25.5 million and $10.2 million for the years ended December 31, 2017, 2016 and 2015, respectively. In addition, as of December 31, 2017, the Company had an accumulated deficit of $96.8 million. The Company expects to continue to generate operating losses for the foreseeable future. As of the issuance date of the annual consolidated financial statements, the Company expects that its cash and cash equivalents, would be sufficient to fund its operating expenses, capital expenditure requirements through at least 12 months from the issuance date of these annual consolidated financial statements. However, the future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its future operations. The Company will seek additional funding through public or private financings, debt financing, collaboration agreements or government grants. The inability to obtain funding, as and when needed, would have a negative impact on the Company's financial condition and ability to pursue its business strategies. If the Company is unable to obtain funding, the Company 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 adversely affect its business prospects, or the Company may be unable to continue operations. Although management intends to pursue plans to obtain additional funding to finance its operations, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

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 common shares prior to the Company's IPO, 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. On an ongoing basis, management evaluates its estimates, 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, 2016, the Company consolidated the following subsidiaries that were not wholly owned:

Subsidiary	Relationship	Country Domiciled	Year of Inclusion
Spero Potentiator, Inc.	Controlling interest	United States	2014
Spero Europe, Ltd.	Controlling interest	United Kingdom	2015
Spero Gyrase, Inc.	Controlling interest	United States	2016
Spero Cantab, Inc.	Controlling interest	United States	2016

All of the non-controlling interests in Spero Europe, Ltd., Spero Potentiator, Inc. and Spero Cantab, Inc. were repurchased by the Company during the year ended December 31, 2017 (see Note 9).

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. Cash equivalents consisted of money market funds at December 31, 2017. The Company did not have any cash equivalents as of December 31, 2016.

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
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.

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. The Company did not record any impairment losses on long-lived assets during the years ended December 31, 2017, 2016 or 2015.

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.

Classification and Accretion of Bridge Units and Redeemable Convertible Preferred Shares

The Company has classified bridge units and redeemable convertible preferred shares outside of stockholders' equity (deficit) because the shares contain certain redemption features that are not solely within the control of the Company. The carrying values of these instruments are accreted to their respective redemption values from the date of issuance through the earliest date of redemption.

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.

Government Contracts and Revenue Recognition

The Company generates revenue from government contracts that reimburse the Company for certain allowable costs for funded projects. For contracts with government agencies, when the Company has concluded that it is the principal in conducting the research and development expenses and where the funding arrangement is considered central to the Company's ongoing operations, the Company classifies the recognized funding received as revenue.

The Company has concluded to recognize funding received from the U.S. Department of Defense ("DoD"), the National Institute of Allergy and Infectious Diseases ("NIAID") of the National Institutes of Health ("NIH") and Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator ("CARB-X") as revenue, rather than as a reduction of research and development expenses, because the Company is the principal in conducting the research and development activities and these contracts are central to its ongoing operations. Revenue is recognized as the qualifying expenses related to the contracts are incurred. Revenue recognition commences only once persuasive evidence of a contract exists, services have been rendered, the reimbursement amounts under the contract are fixed or determinable, and collectibility is reasonably assured. Revenue recognized upon incurring qualifying expenses in advance of receipt of funding is recorded in the Company's consolidated balance sheet as other receivables. The related costs incurred

by the Company are included in research and development expense in the Company's consolidated statements of operations and comprehensive loss.

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 14). 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.

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 2014, the Company entered into a research and development services and support agreement with Hoffmann-La Roche Inc. and certain of its affiliates ("Roche") and concluded that the agreements were not within the scope of the accounting guidance for collaboration arrangements (see Note 13). Due to the co-funded nature of the payments and the Company's assessment that it did not have a vendor/customer relationship with Roche, the Company recognized the nonrefundable payments received under the agreement as a reduction to the research and development expenses incurred, based on a proportional methodology comparing the total expenses incurred in the period under the project to the total expenses expected to be incurred under the project. The Company terminated the agreement with Roche in August 2016.

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 salaries, share-based compensation and benefits, facilities costs, depreciation, manufacturing expenses and external costs of outside vendors engaged to conduct preclinical development activities and 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. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed.

Research Contract Costs and Accruals

The Company has entered into various research and development contracts with research institutions 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. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes 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. Generally, the Company issues awards with only service-based vesting conditions and records the expense for these awards using the straight-line method.

For share-based awards granted to non-employee consultants, compensation expense is recognized over the period during which services are rendered by such consultants until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of the Company's common shares and updated assumption inputs in the Black-Scholes option-pricing model.

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. There was no difference between net loss and comprehensive loss for each of the periods presented in the accompanying consolidated financial statements.

Net Income (Loss) per Share Attributable to Spero Therapeutics, Inc.

The Company follows the two-class method when computing net income (loss) per share, as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed. Net income (loss) per share attributable to common stockholders is calculated based on net income (loss) attributable to Spero Therapeutics, Inc. and excludes net income (loss) attributable to non-controlling interests.

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

The Company's preferred stock contractually entitles the holders of such shares to participate in dividends but does not contractually require the holders of such shares to participate in losses of the Company. Accordingly, in periods in which the Company reports a net loss, such losses are not allocated to such participating securities. In periods in which the Company reports a net loss attributable to common stockholders of Spero Therapeutics, Inc., diluted net loss per share attributable to common stockholders of Spero Therapeutics, Inc. is the same as basic net loss per share attributable to common stockholders of Spero Therapeutics, Inc., since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. The Company reported a net loss attributable to common stockholders of Spero Therapeutics, Inc. for the years ended December 31, 2017, 2016 and 2015.

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 Adopted Accounting Pronouncements

In August 2014, the Financial Accounting Standards Board ("FASB") issued ASU No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern* ("ASU 2014-15"). The amendments in this update explicitly require a company's management to assess an entity's ability to continue as a going concern and to provide related footnote disclosures in certain circumstances. The new standard is effective for annual periods ending after December 15, 2016 and for interim periods thereafter. The Company adopted ASU 2014-15 as of the required effective date of December 31, 2016. This guidance relates to footnote disclosure only, and its adoption had no impact on the Company's financial position, results of operations or cash flows.

In November 2014, the FASB issued ASU No. 2014-16, *Determining Whether the Host Contract in a Hybrid Financial Instrument Issued in the Form of a Share Is More Akin to Debt or to Equity* ("ASU 2014-16"). The guidance requires an entity to determine the nature of the host contract by considering all stated and implied substantive terms and features of the hybrid financial instrument, weighing each term and feature on the basis of the relevant facts and circumstances (commonly referred to as the whole-instrument approach). The Company adopted the standard retrospectively to all periods presented on the required effective date of January 1, 2016, and its adoption had no impact on the Company's financial position, results of operations or cash flows.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes* ("ASU 2015-17"), which requires deferred tax liabilities and assets to be classified as non-current in the consolidated balance sheet. ASU 2015-17 is required to be adopted for annual periods beginning after December 15, 2016, including interim periods within those fiscal years. The amendment may be applied either prospectively to all deferred tax liabilities and assets or retrospectively to all periods presented. The Company elected to early adopt the standard on January 1, 2016 and has reflected the adoption retrospectively to all periods presented. The adoption of ASU 2015-17 had no material impact on the Company's financial position, results of operations or cash flows.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"). ASU 2016-09 involves several aspects of the accounting for share-based transactions, including the income tax consequences, classification of awards as either equity or liabilities, an option to recognize gross share compensation expense with actual forfeitures recognized as they occur and certain classifications on the statement of cash flows. Certain of these changes are required to be applied retrospectively, while other changes are required to be applied prospectively. The Company adopted ASU 2016-09 as of the required effective date of January 1, 2017 and has elected to account for forfeitures as they occur rather than apply an estimated forfeiture rate to share-based compensation expense. The adoption of ASU 2016-09 had no material impact on the Company's financial position, results of operations or cash flows.

Recently Issued Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers (Topic 606)* ("ASU 2014-09"), which supersedes existing revenue recognition guidance under GAAP. The standard's core principle is that a company will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. The standard outlines a five-step process to achieve this principle, and will require companies to use more judgment and make more estimates than under the current guidance. The Company expects that these judgments and estimates will include identifying performance obligations in the customer contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each separate performance obligation. ASU 2014-09 also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts. In August 2015, the FASB issued ASU 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, which delays the effective date of ASU 2014-09 such that the standard is effective for public entities for annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. In March 2016, the FASB issued ASU No. 2016-08, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations* ("ASU 2016-08"), which further clarifies the implementation guidance on principal versus agent considerations in ASU 2014-09. In April 2016, the FASB issued ASU No. 2016-10, *Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing*, clarifying the implementation guidance on identifying performance obligations and licensing. Specifically, the amendments in this update reduce the cost and complexity of identifying promised goods or services and improve the guidance for determining whether promises are separately identifiable. The amendments in this update also provide implementation guidance on determining whether an entity's promise to grant a license provides a customer with either a right to use the entity's intellectual property (which is satisfied at a point in time) or a right to access the entity's intellectual property (which is satisfied over time). In May 2016, the FASB issued ASU No. 2016-12, *Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients* ("ASU 2016-12"), which clarifies the objective of the collectability criterion, presentation of taxes collected from customers, non-cash consideration, contract modifications at transition, completed contracts at transition and how guidance in ASU 2014-09 is retrospectively applied. ASU 2016-08, ASU 2016-10 and ASU 2016-12 have the same effective dates and transition requirements as ASU 2014-09. The Company plans to adopt this standard using the modified retrospective approach. The Company's preliminary assessment is that government grant revenue is outside the scope of ASC 606. Therefore, the Company does not believe the adoption of ASC 606 will impact the Company's financial position, results of operations or cash flows as its only existing revenue source as of December 31, 2017 is government grants.

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). The new standard requires lessees to apply a dual approach, classifying 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, respectively. A lessee is also required to record a right-of-use 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 today. 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 is currently evaluating the impact the adoption of ASU 2016-02 will have on its consolidated financial statements.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15"), to address diversity in practice in how certain cash receipts and cash payments are presented and classified in the statement of cash flows. The standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. The Company does not believe that the adoption of ASU 2016-15 will have a material impact on its consolidated financial statements.

In November 2016, the FASB issued ASU 2016-18 *Statement of Cash Flows (Topic 230)* ("ASU 2016-18"), which requires that amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 is effective for fiscal years beginning after December 15, 2017 and interim periods within those fiscal years and should be applied using a retrospective transition method to each period presented. Early adoption is permitted. The Company does not believe the adoption of ASU 2016-18 will have a material impact on its consolidated financial statements.

In January 2017, FASB issued ASU No. 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business* ("ASU 2017-01"). The amendments in this update clarify the definition of a business with the objective of adding guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions or disposals of assets or businesses. The definition of a business affects many areas of accounting including acquisitions, disposals, goodwill and consolidation. The standard is

effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. The Company does not believe the adoption of ASU 2017-01 will materially impact its consolidated financial statements.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"), which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. The standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. Early adoption is permitted. The Company does not believe the adoption of ASU 2017-09 will materially impact its consolidated financial statements.

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 is currently evaluating the impact that the adoption of ASU 2017-11 will have on its consolidated financial statements.

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, 2017 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ —	$ 83,121	$ —	$ 83,121
	$ —	$ 83,121	$ —	$ 83,121
Liabilities:				
Derivative liabilities:				
Anti-dilution rights	$ —	$ —	$ 223	$ 223
	$ —	$ —	$ 223	$ 223

	Fair Value Measurements at December 31, 2016 Using:			
	Level 1	Level 2	Level 3	Total
Liabilities:				
Derivative liabilities:				
Anti-dilution rights	$ —	$ —	$ 1,806	$ 1,806
Contingent prepayment option	—	—	902	902
	$ —	$ —	$ 2,708	$ 2,708

During the years ended December 31, 2017 and 2016, there were no transfers between Level 1, Level 2 and Level 3.

Tranche Rights

The Company's sales of Class A-1 preferred units ("Class A preferred units") and Class B-1 preferred units ("Class B preferred units") (see Note 6) provided investors with the right to participate in subsequent offerings of Class A and Class B preferred units in the event specified development and regulatory milestones were achieved. The Company classified each of the tranche rights as a derivative liability on its consolidated balance sheet because they met the definition of freestanding financial instruments that could have required the Company to transfer assets upon exercise. The Company remeasured the derivative liabilities associated with tranche rights to fair value at each reporting date, and recognized changes in the fair value of the derivative liabilities 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 the probability-weighted expected return method ("PWERM"), which considered as inputs the probability and time that a milestone would be achieved, the potential fair value of preferred stock upon the exercise of the tranche right and the risk-adjusted discount rate.

Class A Tranche Rights

The fair value of the tranche right related to the Company's Class A preferred unit financing (see Note 6) upon issuance in June 2015 was $2.4 million, which increased slightly as of December 31, 2015. Upon the issuance of the Class B preferred units in February 2016, the tranche right was cancelled and the settlement of the fair value of the derivative liability of $2.4 million was recorded as an increase to additional paid-in capital as a deemed capital contribution from the Class A preferred unit investors.

Class B Tranche Rights

The fair value of the tranche right related to the Company's Class B preferred unit financing upon issuance in February 2016 was $0.9 million. Upon the issuance of bridge units in December 2016, the tranche rights were cancelled and the fair value of the derivative liability, which had decreased by $0.6 million to $0.3 million as of the date of settlement due to a decrease in the fair value of the Company's underlying units, was settled (see Note 6).

Anti-Dilution Rights

In connection with the issuance of non-controlling interests in certain of the Company's subsidiaries (see Note 9), specifically Spero Potentiator, Inc., Spero Europe, Ltd. and Spero Gyrase, Inc., the Company granted anti-dilution rights to the minority investors. The Company classifies the anti-dilution rights as a derivative liability on its consolidated balance sheet because they are freestanding instruments that represent a conditional obligation to issue a variable number of shares. The Company remeasures the derivative liability associated with the anti-dilution rights to fair value at each reporting date, and recognizes 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.

Spero Potentiator

In connection with the Company's issuance of a non-controlling interest in its subsidiary, Spero Potentiator Inc. ("Spero Potentiator"), to Northern Antibiotics Oy Ltd. ("Northern") in February 2015, the Company granted to Northern certain anti-dilution rights (see Note 9). The fair value of the derivative liability related to the anti-dilution rights upon issuance in February 2015 was $2.4 million.

In November 2015, the Company issued an additional 2,736 shares of Spero Potentiator's common shares for no additional cost to Northern as a result of the anti-dilution rights. Upon issuance, the fair value of the additional shares of Spero Potentiator issued to Northern of $1.5 million was recorded as a reduction of the derivative liability and as an increase to the non-controlling interest. In January and August 2016, the Company issued an additional 2,160 shares of Spero Potentiator's common shares for no additional cost to Northern as a result of the anti-dilution rights. Upon issuance, the fair value of the additional shares of Spero Potentiator issued to Northern of $1.0 million was recorded as a reduction of the derivative liability and as an increase to the non-controlling interest. At that time, the derivative liability related to the anti-dilution rights issued to Northern was fully settled as Northern had received the maximum number of shares it was entitled to under the anti-dilution rights.

The most significant assumption impacting the fair value of the anti-dilution rights was the probability that the Company would fund the maximum amount of investment providing anti-dilution protection. Upon issuance of the rights and through August 2016, the date the maximum anti-dilution protection was reached, the Company's assumption for the probability of such funding was 100%.

Spero Europe, Ltd.

In January 2016, in connection with the issuance of a non-controlling interest in its subsidiary, Spero Europe, Ltd. ("Spero Europe"), to Promiliad Biopharma Inc. ("Promiliad"), the Company granted to Promiliad certain anti-dilution rights (see Note 9). The fair value of the derivative liability related to the anti-dilution rights upon issuance in January 2016 was $0.2 million.

The change in the fair value of the derivative liability associated with the anti-dilution rights was insignificant during the year ended December 31, 2016. During 2017, the fair value of the derivative liability decreased by $0.2 million to $0 by May 2017. In May 2017, the non-controlling interest in Spero Europe, Ltd. was repurchased and the anti-dilution rights were settled.

The most significant assumption impacting the fair value of the anti-dilution rights was the probability that the Company would fund the maximum amount of investment providing anti-dilution protection. Upon the issuance of the rights and through December 31, 2016, the probability of such funding was determined to be 100%. During 2017, the probability of funding Spero Europe, Ltd. was reduced to 0% due to the Company's decision to no longer pursue development of the licensed technology.

Spero Gyrase, Inc.

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 Aviragen Therapeutics, Inc.) ("Aviragen"), the Company granted to Aviragen certain anti-dilution rights (see Note 9). The fair value of the derivative liability related to the anti-dilution rights upon issuance in March 2016 was $1.6 million.

The change in the fair value of the derivative liability associated with the anti-dilution rights was insignificant during the year ended December 31, 2016. During 2017, the fair value of the derivative liability decreased by $1.4 million to $0.2 million by June 30, 2017, and remained unchanged as of December 31, 2017.

The most significant assumption impacting the fair value of the anti-dilution rights was the probability that the Company would fund the maximum amount of investment providing anti-dilution protection. Upon issuance of the rights and through December 31, 2016, the probability of such funding was determined to be 100%. During 2017, the probability of such funding was reduced to 0% due to the Company's decision to no longer pursue development of the acquired technology. As of December 31, 2017, the value of the derivative liability of $0.2 million represents amounts funded to the entity that could be settled by the issuance of equity.

Contingent Prepayment Options

Bridge units issued to investors in January 2015 and December 2016 contained contingent prepayment options whereby such units were automatically convertible into equity units sold in a subsequent round of qualified financing at a discounted rate. The Company classified the contingent prepayment options as derivative liabilities on its consolidated balance sheet because the bridge units were deemed to be more akin to debt than equity and the embedded prepayment options were at a substantial discount, thus meeting the definition of derivative liabilities. The Company remeasured the derivative associated with the contingent prepayment options to fair value at each reporting date, and recognized changes in the fair value of the derivative liabilities as a component of other income (expense) in its consolidated statement of operations and comprehensive loss.

The fair value of these derivative liabilities was determined using the PWERM, which considered as inputs the probability and time that a subsequent round of preferred stock financing would occur and the risk-adjusted discount rate.

January 2015 Bridge Units

The fair value of the derivative liability related to the contingent prepayment option associated with bridge units issued in January 2015 was $2.3 million. The option was settled in June 2015 upon the issuance of Class A preferred units. As a condition to the June 2015 financing, the Company and the holders of the bridge units agreed to reduce the previously agreed-upon discount to the per unit conversion price from 20% to 10% of the per unit price of $3.90 to be paid for the sale of the Class A preferred units. The reduction of the discount resulted in a decrease to the fair value of the derivative liability of $1.4 million, which was recorded as an increase to additional paid-in capital as a deemed capital contribution by the holders of the bridge units. The remaining fair value of the derivative liability of $0.9 million was settled upon conversion of the bridge notes into Class A preferred units.

December 2016 Bridge Units

The fair value of the derivative liability related to the contingent prepayment option associated with bridge units issued in December 2016 was $0.9 million. The change in the fair value of the derivative liability associated contingent prepayment option was not material during the year ended December 31, 2016. The fair value of the derivative liability increased by less than $0.1 million as of March 2017, at which time the contingent prepayment option was settled upon the issuance of Class C preferred units.

Investment Option

The Company's concluded collaboration agreement provided its collaboration partner with an option to participate in the next round of financing subsequent to April 2014 in an amount up to $2.0 million at 90.0% of the per unit price of the related financing.

The Company classified the investment option as a derivative liability on its consolidated balance sheet because it met the definition of a freestanding financial instrument that may require the Company to transfer assets upon exercise. The Company remeasured the derivative liability 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 the derivative liability related to the investment option was $0.2 million as of December 31, 2014.

The fair value of the derivative liability associated with investment option decreased by $0.1 million as of June 2015, at which time the subsequent financing occurred and the collaboration partner elected not to exercise the investment option, which then expired. Upon expiration, the Company recorded other income equal to the fair value of the derivative liability upon expiration of $0.1 million.

The fair value of this derivative liability was determined using the PWERM, which considered as inputs the probability and time that a qualified round of preferred stock financing would occur and the risk-adjusted discount rate.

The following table provides a roll forward of the aggregate fair values of the Company's derivative liabilities, for which fair value was determined by Level 3 inputs (in thousands):

	Contingent Prepayment Options	Tranche Rights	Anti-Dilution Rights	Total
Balance at December 31, 2015	$ —	$ 2,404	$ 980	$ 3,384
Fair value at issuance	908	909	1,780	3,597
Change in fair value	(6)	(600)	26	(580)
Settlement	—	(2,713)	(980)	(3,693)
Balance at December 31, 2016	902	—	1,806	2,708
Change in fair value	42	—	(1,583)	(1,541)
Settlement	(944)	—	—	(944)
Balance at December 31, 2017	$ —	$ —	$ 223	$ 223

4. Property and Equipment, Net

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

	December 31,	
	2017	2016
Laboratory equipment	$ 510	$ 484
Computer software and equipment	181	185
Office furniture and equipment	201	201
Leasehold improvements	915	920
	1,807	1,790
Less: Accumulated depreciation and amortization	(643)	(290)
	$ 1,164	$ 1,500

Depreciation and amortization expense was $0.4 million, $0.3 million and less than $0.1 million for the years ended December 31, 2017, 2016 and 2015, respectively.

5. Accrued Expenses and Other Current Liabilities

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

	December 31,	
	2017	2016
Accrued external research and development expenses	$ 1,770	$ 627
Accrued payroll and related expenses	1,369	1,018
Accrued professional fees	878	1,062
Accrued other	304	221
	$ 4,321	$ 2,928

6. Redeemable Convertible Preferred Shares

As of December 31, 2016, the operating agreement of Spero Therapeutics, LLC, as amended and restated, provided for the issuance of Junior preferred units, Class A preferred units, Class B preferred units and bridge units, but did not specify an authorized number of each for issuance. Subsequent to the Reorganization (see Note 1), the Company's amended and restated certificate of incorporation authorized the issuance of 43,297,267 shares of preferred stock, par value $0.001 per share.

2015 Bridge Units

In January 2015, the Company issued and sold 8,000 bridge units to existing investors at a price of $1,000 per unit for gross proceeds of $8.0 million (the "2015 bridge units"). The bridge units did not have any stated rate of return and were automatically convertible into the same type of units issuable upon a qualified financing at a discount of either 20.0% or 25.0% to the per unit price paid by investors in a qualified financing, depending on the timing of such financing. The Company classified this contingent prepayment option as a derivative liability on its consolidated balance sheet on the date of issuance (see Note 3), and the fair value of contingent prepayment option on the date of issuance of $2.3 million was recorded as both a derivative liability and as a reduction to the carrying value of the bridge units.

Class A Preferred Unit Financing

In June 2015, the Company issued and sold 1,923,076 Class A preferred units at a price of $3.90 per unit for proceeds of $7.3 million, net of issuance costs of $0.2 million. The sale of Class A preferred units met the definition of a qualified financing under the 2015 bridge unit agreements.

As a condition to the June 2015 Class A preferred unit financing, the Company and the holders of the 2015 bridge units agreed to reduce the previously agreed-upon discount to the per unit conversion price from 20% to 10% of the price to be paid for the sale of Class A preferred units of $3.90 per unit. Accordingly, the Company issued 2,279,202 Class A preferred units upon the conversion of the 2015 bridge units in the amount of $8.0 million, at a conversion price of $3.51 per unit. The conversion was accounted for as an extinguishment for accounting purposes. Accordingly, the Company recorded the Class A preferred units issued upon conversion of the 2015 bridge units at their aggregate fair value of $8.9 million and recorded a corresponding adjustment to extinguish the then-

current carrying value of the 2015 bridge units of $8.0 million and the then-current fair value of the derivative liability related to the contingent prepayment option associated with the 2015 bridge units of $0.9 million (see Note 3). There was no gain or loss recognized upon the extinguishment.

The Class A preferred unit financing included a provision for the issuance of an additional 3,295,455 Class A preferred units at a price of $4.40 per unit in exchange for gross proceeds of $14.5 million in the event the Company achieved a regulatory milestone. The Company classified this tranche right as a derivative liability on its consolidated balance sheet on the date of issuance, and the fair value of tranche right on the date of issuance of $2.4 million was recorded as both a derivative liability and as a reduction to the carrying value of the Class A preferred units. Upon issuance of the Class B preferred units in February 2016, the tranche right was cancelled (see Note 3).

Class B Preferred Unit Financing

In February 2016, the Company issued and sold 5,909,089 Class B preferred units at a price of $4.40 per unit for proceeds of $25.9 million, net of issuance costs of $0.1 million.

The Class B preferred unit financing included a provision for the issuance of an additional 1,609,846 Class B preferred units at a price of $5.28 per unit in exchange for gross proceeds of $8.5 million in the event the Company achieved a regulatory milestone. The Company classified this tranche right as a derivative liability on its consolidated balance sheet on the date of issuance, and the fair value of the tranche right on the date of issuance of $0.9 million was recorded as both a derivative liability and as a reduction to the carrying value of the Class B preferred units.

2016 Bridge Units

The regulatory milestone related to the Class B tranche right was achieved in the fourth quarter of 2016; however, the Company and the holders of the Class B preferred units agreed to replace the second closing of Class B preferred units with the issuance of bridge units that would be convertible in the next qualified financing at a 10% discount. Accordingly, in December 2016, the Company issued and sold 8,500 bridge units to existing investors at a price of $1,000 per unit for gross proceeds of $8.5 million (the "2016 bridge units"). Upon issuance of the 2016 bridge units, the fair value of the derivative liability associated with the Class B tranche right of $0.3 million was settled, resulting in a decrease to the carrying value of the derivative liability and an increase to the carrying value of the 2016 bridge units (see Note 3). The bridge units did not provide for any stated rate of return and were automatically convertible into the same type of units issuable upon a qualified financing at a 10% discount to the per unit price paid by investors in a qualified financing. The Company classified this contingent prepayment option as a derivative liability on its consolidated balance sheet on the date of issuance, and the fair value of the contingent prepayment option on the date of issuance of $0.9 million was recorded as both a derivative liability and as a reduction to the carrying value of the bridge units.

Class C Preferred Unit Financing

In March 2017, the Company issued and sold 24,326,470 Class C preferred units at a price of $1.7749 per unit for proceeds of $43.0 million, net of issuance costs of $0.2 million. The sale of Class C preferred units met the definition of a qualified financing under the 2016 bridge unit agreements.

The Company issued 5,321,112 Class C preferred units upon the conversion of the 2016 bridge units in the amount of $8.5 million, at a conversion price of $1.60 per unit, which represented a discount of 10% to the price per unit paid by other investors in the Class C preferred unit financing. The conversion was accounted for as an extinguishment for accounting purposes. Accordingly, the Company recorded the Class C preferred units issued upon conversion of the 2016 bridge units at their aggregate fair value of $9.4 million and recorded a corresponding adjustment to extinguish the then-current carrying value of the 2016 bridge units of $8.5 million and the then-current fair value of the derivative liability related to the contingent prepayment option associated with the 2016 bridge units of $0.9 million (see Note 3). There was no gain or loss recognized upon the extinguishment.

In July 2017 the Company sold to its Chief Financial Officer 61,880 shares of the Company's Series C preferred stock at a price of $1.7749 per share, for proceeds of $0.1 million.

Shares of Preferred Stock of Spero Therapeutics, Inc. Issued upon the Reorganization

On June 30, 2017, pursuant to the terms of the Reorganization (see Note 1), holders of outstanding preferred units of Spero Therapeutics, LLC exchanged their units for preferred stock of Spero Therapeutics, Inc. on a one-for-one basis. The rights and preferences of each class of stock (as described below) were the same both before and after the Reorganization. Upon the closing of

the Company's IPO in November 2017, all of the then outstanding convertible preferred shares automatically converted into shares of common stock (see Note 7).

The Junior preferred stock, the Series A preferred stock, the Series B preferred stock and the Series C preferred stock are collectively referred to as the "Preferred Stock". The holders of the Preferred Stock have the following rights and preferences:

Voting

The holders of Preferred Stock are entitled to vote, together with the holders of common stock, on all matters submitted to stockholders for a vote. The holders of Preferred Stock are entitled to the number of votes equal to the number of common shares into which each such share of Preferred Stock could convert.

Conversion

Each share of Preferred Stock is convertible at the option of the holder at any time after the date of issuance. Each share of Preferred Stock would be automatically converted into shares of common stock at the applicable conversion ratio then in effect (i) upon the closing of a firm commitment public offering with at least $50.0 million of proceeds to the Company or (ii) upon the written consent of the holders of at least 60% of the then-outstanding shares of Series B and Series C preferred stock, voting together as a single class.

The conversion ratio of each series of Preferred Stock is determined by dividing the Original Issue Price of each series by the Conversion Price of each series. The Original Issue Price is $1.00 per share for Junior preferred stock, $3.90 per share for Series A preferred stock, $4.40 per share for Series B preferred stock and $1.7749 per share for Series C preferred stock. The Conversion Price at issuance was $6.0774 per share for Junior preferred stock, $23.7019 per share for Series A preferred stock, $26.7406 per share for Series B preferred stock and $10.7868 per share for Series C preferred stock, subject to appropriate adjustment in the event of any stock split, stock dividend, combination or other similar recapitalization and other adjustments as set forth in the Company's certificate of incorporation, as amended and restated. In March and July 2017, as a result of the issuances of Series C preferred stock at a price per share less than the Series A and Series B preferred stock Conversion Price, the Conversion Price for each of Series A and Series B preferred stock was adjusted according to their terms. Prior to the Company's Reorganization in June 2017, the Conversion Price of Series A and Series B preferred stock was $15.5715 per share and $16.7256 per share, respectively. The Conversion Price for Junior preferred stock was not adjusted according to its terms. In July 2017, after the consummation of the Reorganization, the Company sold to its Chief Financial Officer 61,880 shares of the Company's Series C preferred stock at a price of $1.7749 per share, for proceeds of $0.1 million. Because the price per share of the Series C preferred stock in this transaction was lower than the Conversion Price of the Company's Series A and Series B preferred stock, in accordance with the Company's certificate of incorporation, as amended and restated, the Conversion Price of Series A preferred stock was adjusted from $15.5715 to $15.5654 per share and the Conversion Price of Series B preferred stock was adjusted from $16.7256 to $16.7177 per share. The Conversion Price for Junior preferred stock was not adjusted according to its terms.

On October 20, 2017, the Company effected a one-for-6.0774 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion rations for each series or the Company's Preferred Stock. Upon the closing of the Company's IPO in November 2017, the Company's outstanding preferred shares automatically converted into shares of common stock.

Dividends

Holders of the Series A, Series B and Series C preferred stock are entitled to receive, out of funds legally available, cumulative dividends at an annual rate of 8%, compounded annually, when and if declared by the board of directors. Holders of the Junior preferred stock are entitled to receive, out of funds legally available, noncumulative dividends at an annual rate of 5%, when and if declared by the board of directors. The Company may not declare, pay or set aside any dividends on shares of any other series of capital stock of the Company, other than dividends on common stock payable in common stock, unless the holders of the Series C preferred stock first receive, or simultaneously receive, a dividend on each outstanding share of Series C preferred stock to which they are entitled. The Company may not declare, pay or set aside any dividends on shares of any other series of capital stock of the Company, other than dividends on shares of Series C preferred stock and dividends on common stock payable in common stock, unless the holders of the Series B preferred stock first receive, or simultaneously receive, a dividend on each outstanding share of Series B preferred stock to which they are entitled. The Company may not declare, pay or set aside any dividends on shares of any other series of capital stock of the Company, other than dividends on shares of Series B preferred stock or Series C preferred stock and dividends on common stock payable in common stock, unless the holders of the Series A preferred stock first receive, or simultaneously receive, a dividend on each outstanding share of Series A preferred stock to which they are entitled. The Company may not declare, pay or set aside any dividends on shares of any other series of capital stock of the Company, other than dividends on

shares of Series A, Series B or Series C preferred stock and dividends on common stock payable in common stock, unless the holders of the Junior preferred stock first receive, or simultaneously receive, a dividend on each outstanding share of Junior preferred stock to which they are entitled. Through December 31, 2017 and 2016, no cash dividends have been declared or paid by the Company's board of directors.

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution or winding-up of the Company or Liquidating Event (as described below), the holders of shares of Preferred Stock will receive, in preference to the common stockholders, an amount equal to the greater of (i) the Original Issue Price per share of the respective share of preferred stock, plus all dividends declared but unpaid on such shares or (ii) the amount the holders would receive if the Preferred Stock were converted into common stock prior to such liquidation event. If, upon any such liquidation event, the assets of the Company available for distribution are insufficient to permit payment in full to the holders of Preferred Stock, the holders of the Series C preferred stock are entitled to receive such amount prior to and in preference of the holders of the Series B, Series A, Junior preferred stock and common stock. After payment in full to holders of Series C preferred stock, the holders of the Series B preferred stock are entitled to receive such amount prior to and in preference of the holders of the Series A, Junior preferred stock and common stock. After payment in full to holders of Series C and Series B preferred stock, the holders of the Series A preferred stock are entitled to receive such amount prior to and in preference of the holders of the Junior preferred stock and common stock. After payment in full to holders of Series C, Series B and Series A preferred stock, the holders of the Junior preferred stock are entitled to receive such amount prior to and in preference of the holders of the common stock. In the event that the assets available for distribution to the Company's stockholders are not sufficient to permit payment to any class of holders in order of preference and in the full amount to which they are entitled, the assets available for distribution are distributed on a pro rata basis. In addition, solely if (i) proceeds are received in connection with the sale or merger of Spero Potentiator, Inc. and (ii) contracted distribution thresholds in relation to anti-dilution clauses are satisfied, then distributions to the Series A holders shall be made until their Adjusted Potentiator Shortfall Amount, as defined, is met, after payments to Series C and Series B preferred stock have been made in full but prior to and in preference of the holders of the Junior preferred stock and common stock. After the payment of all preferential amounts to the holders of the Preferred Stock then, to the extent available, the remaining assets available for distribution shall be distributed among the holders of the Preferred Stock and common stock ratably in proportion to the number of shares of stock held as converted to common stock.

Unless the holders of 60% of the then-outstanding shares of Series B and Series C preferred stock, voting together as a single class, and holders of 60% of the then-outstanding shares of Series C preferred stock elect otherwise, a Liquidating Event shall include a merger or consolidation (other than one in which stockholders of the Company own a majority by voting power of the outstanding shares of the surviving or acquiring corporation) or a sale, lease, transfer, exclusive license or other disposition of all or substantially all of the assets of the Company.

Redemption

At any time on or after February 1, 2021, shares of each of the Junior preferred stock, Series A, Series B and Series C preferred stock are subject to mandatory redemption by the Company in three equal annual installments beginning 60 days after receipt of a notice of redemption from the holders of at least 60% of the combined voting power of the holders of the outstanding Series B and Series C preferred stock, voting as a single class at the Original Issue Price, subject to appropriate adjustment for any stock splits, stock dividends, combinations or any other similar recapitalization affecting such shares, plus any dividends declared but unpaid thereon plus cumulative dividends. If, upon any such redemption, the assets of the Company available for distribution are insufficient to permit payment in full to the holders of Preferred Stock, the holders of the Series C preferred stock are entitled to receive such amount prior to and in preference of the holders of the Series B, Series A and Junior preferred stock. After payment in full to holders of Series C preferred stock, the holders of the Series B preferred stock are entitled to receive such amount prior to and in preference of the holders of the Series A and Junior preferred stock. After payment in full to holders of Series C and Series B preferred stock, the holders of the Series A preferred stock are entitled to receive such amount prior to and in preference of the holders of the Junior preferred stock. In the event that the assets are not sufficient to permit payment of the redemption amount to any class of holders in order of preference and in the full amount to which they are entitled, the assets available for distribution are distributed on a pro rata basis.

7. Common Stock

As of December 31, 2016, the operating agreement of Spero Therapeutics, LLC, as amended and restated, provided for the issuance of common units, but did not specify an authorized number for issuance.

Subsequent to the Reorganization on June 30, 2017 (see Note 1), the Company's amended and restated certificate of incorporation authorized the issuance of 61,917,986 shares of common stock, par value $0.001 per share. Subsequent to the Company's IPO on November 6, 2017 (See Note 1), the Company's amended and restated certificate of incorporation authorized the issuance of 60,000,000 shares of common stock, par value $0.001 per share. Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are not entitled to receive dividends, unless declared by the board of directors.

In 2014, the Company issued and sold restricted common units, which were subject to vesting requirements. In 2016, the Company repurchased 21,116 unvested common units upon forfeiture at the original issuance price of $0.001 per unit. As of December 31, 2015 and 2016, there were 75,210 units and 7,062 units, respectively, of unvested restricted common units outstanding. There were no unvested common units outstanding as of December 31, 2017.

On June 30, 2017, pursuant to the terms of the Reorganization (see Note 1), holders of common units of Spero Therapeutics, LLC exchanged their units for common stock of Spero Therapeutics, Inc. on a one-for-one basis. On October 20, 2017, the Company effected a one-for-6.0774 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of the Company's Preferred Stock (see Note 6). Accordingly, all share and per share amounts for all periods presented in the accompanying consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the preferred stock conversion ratios. In addition, all common units and incentive units as well as the conversion ratios of preferred units of Spero Therapeutics, LLC have been presented as if the reverse stock split of the common stock of Spero Therapeutics, Inc. had been applied to such units and ratios of Spero Therapeutics, LLC.

8. Share-Based Compensation

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.

The following table summarizes the Company's incentive unit activity since December 31, 2016:

	Number of Units	Weighted Average Strike Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2016	413,266	$ 2.75	9.1	$ 779
Granted	9,132	1.28	—	—
Exercised	—	—	—	—
Forfeited	(19,541)	4.99	—	—
Cancelled	(402,857)	2.62	—	—
Outstanding as of December 31, 2017	—	$ —	—	$ —

As of December 31, 2016, total unrecognized compensation cost related to the unvested share-based awards was $0.8 million, which was expected to be recognized over a weighted average period of 3.1 years. 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.

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, 2017, there were 685,105 shares remaining available to be issued 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.

Incentive Unit and Stock Option Valuation

The fair value of each incentive unit award and stock options are 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 incentive units 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 incentive unit and stock option awards granted to employees and directors were as follows, presented on a weighted average basis:

	Year Ended December 31,		
	2017	2016	2015
Risk-free interest rate	2.0%	1.3%	1.5%
Expected term (in years)	6.1	6.3	6.3
Expected volatility	77.1%	76.5%	62.6%
Expected dividend yield	0.0%	0.0%	0.0%

The following table summarizes stock option activity during 2017:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2016	—	$ —	—	$ —
Granted	2,012,106	7.24	—	—
Exercised	—	—	—	—
Forfeited	(810)	5.90	—	—
Cancelled	—	—	—	—
Outstanding as of December 31, 2017	2,011,296	$ 7.24	9.38	$ 9,074
Outstanding as of December 31, 2017 - vested and expected to vest	2,011,296	$ 7.24	9.38	$ 9,074
Exercisable at December 31, 2017	357,494	$ 5.90	9.29	$ 2,091

The weighted average grant-date fair value of stock options granted during 2017 was $4.72 per share. No stock options were exercised during 2017. The weighted average grant-date fair value of awards granted during the years ended December 31, 2016 and 2015 was $3.40 per unit and $1.03 per unit, respectively.

As of December 31, 2017, 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 3.4 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,		
	2017	2016	2015
Research and development expenses	$ 371	$ 66	$ 13
General and administrative expenses	1,056	114	8
Total	$ 1,427	$ 180	$ 21

9. Non-Controlling Interests

Spero Potentiator

In February 2015, the Company's wholly owned subsidiary, Spero Potentiator, issued 996 shares of its common stock with an aggregate fair value of $1.1 million to Northern in exchange for an exclusive license to develop and commercialize certain licensed compounds and licensed products. The Company recognized research and development expense of $1.1 million upon acquisition of the license and recorded a non-controlling interest in Spero Potentiator in a corresponding amount.

In connection with the acquisition of the license, Northern obtained anti-dilution rights to maintain its 49.9% ownership percentage in Spero Potentiator at no additional cost to Northern in the event that Spero Potentiator completed subsequent equity financings, subject to a maximum amount of such financings. The maximum amount of gross proceeds from equity financings subject to the anti-dilution rights was $5.0 million through the date the Company filed an investigational new drug application ("IND") related to the licensed technology. Subsequent to the filing of an IND, the maximum amount of gross proceeds from equity financings subject to the anti-dilution rights was $6.5 million.

The Company accounted for the anti-dilution rights as a derivative liability on its consolidated balance sheet (see Note 3). The fair value of the derivative liability associated with the anti-dilution rights upon issuance in February 2015 of $2.4 million was recorded as research and development expenses as it was deemed to represent additional consideration for the license.

In November 2015, Northern was issued an additional 2,736 common shares of Spero Potentiator for no additional cost as a result of the anti-dilution rights. The Company valued these shares at $1.5 million and recorded the amount as an increase in the non-

controlling interest and a reduction in the carrying value of the derivative liability. In January and August 2016, Northern was issued an additional 2,160 common shares of Spero Potentiator for no additional cost. The Company valued these shares at $1.0 million and recorded the amount as an increase in the non-controlling interest and a reduction of the derivative liability. At that time, the anti-dilution rights issued to Northern were fully settled as Northern had received the maximum number of shares it was entitled to under the anti-dilution rights (See Note 3).

In June 2017, the Company repurchased all of the shares of Spero Potentiator held by Northern in exchange for a cash payment of $1.0 million and contingent consideration of $0.1 million. As a condition of the repurchase of the shares from Northern, the Company amended the license agreement with Northern such that the Company will be obligated to make milestone payments of up to $7.0 million upon the achievement of specified clinical, commercial and other milestones, including a payment of $2.5 million upon the closing of an IPO, which occurred and was paid in November 2017. As a result of this transaction, during the six months ended June 30, 2017, the Company reclassified the balance of the non-controlling interest of $6.4 million as of the date of the transaction to accumulated deficit as an increase to that account. Additionally, the cash payment of $1.0 million was recorded as an increase to accumulated deficit. The Company will record the contingent payments as research and development expense when it becomes probable that the payments will be due. For periods subsequent to the acquisition, the Company no longer reports a non-controlling interest related to Spero Potentiator.

Spero Europe

In January 2016, the Company entered into an agreement with Promiliad whereby Promiliad granted to Spero Europe certain know-how and a sublicense to research, develop, manufacture and sell certain compounds. In exchange for the know-how and sublicense, Spero Europe provided Promiliad with a 5% equity ownership interest in Spero Europe, with a fair value of $0.1 million. In addition, Spero Europe agreed to make payments to Promiliad upon the achievement of future regulatory and commercial milestones of $4.1 million and to pay to Promiliad royalties of a mid single-digit percentage on net sales of licensed products under the agreement. Spero had the right to terminate the agreement with thirty days' notice. The Company recognized research and development expense of $0.1 million upon the acquisition of the license and recorded a non-controlling interest in Spero Europe in a corresponding amount.

In connection with the acquisition of the license, Promiliad obtained anti-dilution rights to maintain their 5% equity ownership in Spero Europe at no additional cost to Promiliad in the event that Spero Europe completed subsequent funding events, subject to a maximum amount of such funding of $5.0 million.

The Company accounted for the anti-dilution rights as a derivative liability on its consolidated balance sheet (see Note 3). The fair value of the derivative liability associated with the anti-dilution rights upon issuance in January 2016 of $0.2 million was recorded as research and development expenses as it was deemed to represent additional consideration for the license.

In May 2017, the Company repurchased all of the shares of Spero Europe from Promiliad in exchange for the return of the license. As a result of the transaction, the Company reclassified the balance of the non-controlling interest in Spero Europe of less than $0.1 million as of the date of the transaction to accumulated deficit as an increase to that account. For periods subsequent to the repurchase, the Company no longer reports a non-controlling interest related to Spero Europe.

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 connection with the agreement, Aviragen obtained anti-dilution rights to maintain their 20% equity ownership of Spero Gyrase at no additional cost to Aviragen in the event that Spero Gyrase completed subsequent funding events, subject to a maximum amount of such funding of $8.0 million.

The Company accounted for the anti-dilution rights as a derivative liability on its consolidated balance sheet (see Note 3). The fair value of the derivative liability associated with the anti-dilution rights upon issuance in March 2016 of $1.6 million was recorded as research and development expenses as it was deemed to represent additional consideration for the license.

Spero Cantab

In June 2016, the Company entered into a stock purchase agreement and related agreements (the "Cantab Agreements") with Pro Bono Bio PLC, a corporation organized under the laws of England, and certain of its affiliates, including PBB Distributions Limited ("PBB"), Cantab Anti-Infectives Ltd. ("CAI") and New Pharma License Holdings Limited ("NPLH") in order to acquire NPLH and its intellectual property rights and assets relating to the Company's Potentiator Platform.

Under the Cantab Agreements, CAI agreed to submit a request to NIAID to novate the CAI-held NIAID contract to the Company. The NIAID contract provides for development funding of up to $5.7 million over a base and three option periods. As of December 31, 2017, funding for the base period and the first two option periods totaling $5.1 million had been committed to CAI. Novation of the NIAID contract to the Company was finalized in December 2017. The Company shall pay PBB a percentage of funds received from NIAID up to a maximum of $1.3 million.

Consideration under Cantab Agreements consisted of: (i) 125 shares of Spero Cantab, the Company's subsidiary, which represented a 12.5% ownership interest in Spero Cantab, and anti-dilution rights (as described below) issued to PBB, with a combined fair value of $1.6 million, (ii) upfront consideration of $0.3 million (to be credited against future payments payable to CAI), (iii) contingent milestone payments due upon the achievement of certain clinical, regulatory and commercial milestones (see Note 13), (iv) royalty payments of low single-digit percentages based on net sales of products from the licensed technology, and (v) a specified portion of funding payments made by NIAID.

The Company accounted for the acquisition of NPLH as an asset acquisition because NPLH did not meet the definition of a business. The Company recognized research and development expense of $1.6 million upon the acquisition of NPLH because the acquired technology had not reached commercial feasibility and had no alternative future use. Upon the issuance of the shares and anti-dilution rights, the Company recorded a non-controlling interest in Spero Cantab of $1.6 million. The $0.3 million payment was recognized as research and development expenses as the services were performed by CAI. The Company records the contingent payments outlined in (iii), (iv) and (v) as research and development expense when it becomes probable that the payments will be due. Novation of the NIAID contract to Spero was finalized in December 2017. Prior to the contract novation, CAI performed research and development services at the Company's direction and applied for reimbursement from NIAID. The Company paid CAI for such research and development services at an agreed-upon rate which took into consideration costs incurred by CAI, amounts reimbursed to CAI by NIAID and the portion of the NIAID reimbursement the Company paid to CAI.

In connection with the Cantab Agreements, PBB obtained anti-dilution rights to maintain a certain equity ownership, ranging from 5% to 12.5%, of Spero Cantab at no additional cost to PBB in the event that Spero Cantab completed subsequent funding events, subject to maximum amount of such funding of $8.0 million. These anti-dilution rights represent a conditional obligation to issue a variable number of shares but are not freestanding and, therefore, do not require bifurcation for accounting purposes from the 125 shares issued.

In July 2017, the Company repurchased all of the outstanding shares of Spero Cantab owned by PBB in exchange for a cash payment of $0.2 million and an amendment to the licensing agreement to increase the first two contingent milestone payments by a total of $0.1 million. For periods subsequent to the repurchase, the Company no longer reports a non-controlling interest related to Spero Cantab.

As of each balance sheet date, non-controlling interests' balances were as follows (in thousands):

	December 31,	
Entity	**2017**	**2016**
Spero Potentiator	$ —	$ (5,470)
Spero Europe	—	(21)
Spero Gyrase	355	380
Spero Cantab	—	1,303
	$ 355	$ (3,808)

10. 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, 2017, 2016 and 2015, 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,		
	2017	2016	2015
Domestic	$ (38,706)	$ (27,148)	$ (12,832)
Foreign	$ (1,180)	(5,493)	(321)
Loss before income taxes	$ (39,886)	$ (32,641)	$ (13,153)

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,		
	2017	2016	2015
Federal statutory income tax rate	(34.0)	(34.0)	(34.0)
Federal and state research and development tax credit	(3.3)	(1.7)	(0.9)
State taxes, net of federal benefit	(5.3)	(4.4)	(5.2)
Foreign rate differential	0.1	2.3	0.3
Nondeductible items	(0.1)	4.8	10.2
Effect of US tax reform	23.8	—	—
Increase in deferred tax asset valuation allowance	18.8	33.0	29.6
Effective income tax rate	—	—	—

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

	December 31,	
	2017	2016
Net operating loss carryforwards	$ 21,754	$ 16,406
Research and development tax credit carryforwards	2,022	697
Other	743	49
Total deferred tax assets	24,519	17,152
Valuation allowance	(24,519)	(17,152)
Net deferred tax assets	$ —	$ —

As of December 31, 2017, the Company had U.S. federal and state net operating loss carryforwards of $76.4 million and $76.0 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2033. In addition, as of December 31, 2017, the Company had foreign net operating loss carryforwards of $4.3 million, which may be available to offset future income tax liabilities and do not expire. As of December 31, 2017, the Company also had federal and state research and development tax credit carryforwards of $1.7 million and $0.4 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, 2017 and 2016. 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, 2017 and 2016 related primarily to the increase in net operating loss carryforwards, capitalized research and development expenses and research and development tax credit carryforwards and were as follows (in thousands):

	December 31,	
	2017	2016
Valuation allowance as of beginning of year	$ (17,152)	$ (6,157)
Decreases recorded as benefit to income tax provision	—	—
Increases recorded to income tax provision	(7,367)	(10,995)
Valuation allowance as of end of year	$ (24,519)	$ (17,152)

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2017 or 2016. 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, 2017 and 2016, 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.

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 2013. 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. The Company has recognized the provisional tax impacts related to the revaluation of deferred tax assets and liabilities and included these amounts in its consolidated financial statements for the year ended December 31, 2017. While the Company believes these estimates are

reasonable, the ultimate impact may differ from these provisional amounts due to further review of the enacted legislation, changes in interpretations and assumptions it has made, and additional accounting and regulatory guidance that may be issued.

11. 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 13).

Operating Leases

In August 2015, the Company entered into an operating lease agreement for office space that commenced in January 2016 and expires in December 2020. The lease requires annual payments of $0.4 million over the five-year term. The lease provides for a renewal option to extend the lease for an additional five years. Under the terms of the lease, the Company provided a security deposit of $0.2 million to the landlord, which is included in long-term assets in the accompanying consolidated balance sheets. The lease includes annual rent escalations as well as tenant incentives in the amount of $0.7 million, of which $0.3 million is reimbursed to the landlord over the term of the lease.

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

On January 17, 2018, the Company entered into an amendment (the "Amendment") to the lease agreement with respect to its corporate headquarters located at 675 Massachusetts Avenue, Cambridge, Massachusetts. The Amendment makes certain changes to the original Lease Agreement, dated August 24, 2015 (the "Original Lease"), by and between the Company and U.S. REIF Central Plaza Massachusetts, LLC (the "Landlord"), including (i) the addition of approximately 7,800 square feet of office space in the same building (the "Expansion Premises") and (ii) an extension of the expiration date of the Original Lease to seven years following the delivery date of the Expansion Premises (the "Lease Term"), which is estimated to be December 1, 2018.

Under the 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. The Amendment provides for annual base rent for the Expansion Premises of approximately $0.5 million in the first year of the Lease Term, which increases on an annual basis to approximately $0.6 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.

Rent escalations and tenant incentives for operating leases are included in deferred rent in the consolidated balance sheet, and rent expense is recognized on a straight-line basis over the terms of occupancy.

The following table summarizes the future minimum payments due under the operating leases as of December 31, 2017 (in thousands):

Year Ending December 31,	
2018	$ 820
2019	808
2020	499
2021	—
	$ 2,127

Rent expense for the years ended December 31, 2017, 2016 and 2015 was $0.8 million, $0.4 million and $0.1 million, respectively.

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, 2017, 2016 or 2015.

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.

12. Government Contracts

U.S. Department of Defense

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 year ended December 31, 2017, the Company recognized $0.7 million of revenue under this agreement, of which $0.1 million was invoiced but unpaid and included in other receivables at December 31, 2017. During the year ended December 31, 2016, $0.3 million of revenue was recognized under this agreement, of which $0.3 million was invoiced but unpaid and included in other receivables at December 31, 2016.

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. Through December 31, 2017, only the base period funds had been committed. In February 2018 NIAID exercised the $0.4 million 12-month option period. The Company recognized $0.4 million of revenue in the year ended December 31, 2017 under this agreement, of which less than $0.1 million was invoiced but unpaid and included in other receivables at December 31, 2017.

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 CAI-held NIAID contract to Spero. The NIAID contract provides for development funding of up to $5.7 million over a base period and three option periods. As of December 31, 2017, funding for the base period and the first two option periods totaling $5.1 million have been committed. Novation of the NIAID contract to Spero was finalized in December 2017. Spero shall pay PBB a percentage of funds received from NIAID up to a maximum of $1.3 million.

CARB-X

In April 2017, the Company was awarded a grant from CARB-X, a public-private partnership funded by the Biomedical Advanced Research and Development Authority ("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 Company's lead Potentiator compound. 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 $0.9 million of revenue in the year ended December 31, 2017 under this agreement, of which $0.7 million was invoiced but unpaid and included in other receivables at December 31, 2017.

13. 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.

Roche Collaboration Agreements

In April 2014, the Company and Roche entered into a research and development services and support agreement ("Research and Development Agreement") and an option agreement ("Option Agreement"), whereby the Company was required to use its best efforts to research and develop a specified asset, while Roche would provide partial funding as well as participate on a joint steering committee for the development of this asset. As part of these agreements, the Company provided Roche with the option to participate in the Company's next financing subsequent to April 2014 in an amount up to $2.0 million at 90.0% of the per unit price of the related financing (see Note 3). The subsequent financing occurred in June 2015 and, as Roche elected not to exercise its option, the option expired.

As consideration for the agreements, Roche made nonrefundable upfront payments aggregating to $2.0 million in 2014 and paid annual nonrefundable maintenance fees of $1.0 million in 2015. Due to the cooperative nature of the development plans as driven by the joint steering committee and the partial defrayment of development costs, the nonrefundable payments were considered reductions to research and development expense. Upon receipt, the payments the Company received in 2014 and 2015 from Roche were deferred and were recognized as reductions to research and development expense.

In June 2016, the Company provided notification to Roche that it intended to terminate its Research and Development Agreement with Roche based on its rights under the agreement, effective August 2016, resulting in a recognition of the remaining deferred advance research and development payments. There was no termination fee required under the agreement. Related to payments received under the concluded collaboration, the Company recognized reductions of research and development expense of $0.9 million and $1.5 million for the years ended December 31, 2016 and 2015, respectively.

MGH License Agreement

In March 2014, the Company entered into a license agreement with The General Hospital Corporation, doing business as Massachusetts General Hospital, ("MGH") to obtain an exclusive worldwide license to research, develop, manufacture and sell products based on technology related to inhibitors of bacteria quorum sensing and technology pertaining to the methods for identifying compounds for treating, reducing or preventing pathogenic infections.

Upon signing of the license agreement, the Company issued to MGH 24,681 common units. The Company also agreed to reimburse MGH for all patent costs related to the exclusive patent for the duration of the agreement. In November 2016, the Company terminated its license agreement with MGH. There were no termination payments required.

Ascenion License Agreement

In September 2014, the Company entered into a license agreement with Ascenion GmbH (formerly known as Helmholtz Zentrum fur Infektionsforschung GmbH) to obtain an exclusive worldwide license to research, develop, manufacture and sell products based on Ascenion's PqsR modulator technology. Upon signing of the license agreement, the Company issued to Ascenion 9,625 common units. In November 2016, the Company terminated its license agreement with Ascenion. There were no termination payments required.

Aviragen Agreement

Under the Company's agreement with Aviragen (see Note 9) for certain intellectual property and know-how relating to developing a gyrase inhibitor to develop therapies for Gram-negative infections, the Company is 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.

Cantab License Agreement

Under the Cantab Agreements (see Note 9), 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 ($6.7 million and $6.2 million as of December 31, 2017 and 2016, 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.

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.

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 SPR994. The payment was recorded as research and development expense in the statement of operations and comprehensive loss for the year ended December 31, 2017.

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 SPR994 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 (see Note 9), 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 has 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.

14. 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, 2017 and 2016, $1.8 million and $0.1 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, 2017 and 2016, the Company's tax incentive receivables from the Australian government totaled $1.9 million and $0.1 million, respectively.

15. 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,		
	2017	2016	2015
Numerator:			
Net loss	$ (39,886)	$ (32,641)	$ (13,153)
Less: Net loss attributable to non-controlling interests	(1,143)	(7,150)	(2,999)
Plus: Cumulative dividends on redeemable convertible preferred shares	(6,146)	(3,441)	(932)
Plus: Accretion of bridge units and redeemable convertible preferred shares to redemption value	(1,208)	(996)	(2,341)
Net loss attributable to common stockholders of Spero Therapeutics, Inc.	$ (46,097)	$ (29,928)	$ (13,427)
Denominator:			
Weighted average common shares outstanding, basic and diluted	2,586,865	312,169	252,807
Net loss per share attributable to common stockholders of Spero Therapeutics, Inc., basic and diluted	$ (17.82)	$ (95.87)	$ (53.11)

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:

	December 31,		
	2017	2016	2015
Options to purchase common stock	2,011,296	—	—
Redeemable convertible preferred shares (as converted to common shares)	—	2,229,518	1,257,213
Incentive units	—	413,266	171,758
	2,011,296	2,642,784	1,428,971

16. 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 and to date has not made any contributions to the 401(k) Plan. The Company did not make any matching contributions during the years ended December 31, 2017, 2016 and 2015.

17. Quarterly Financial Data (unaudited)

	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
Grant revenue	$ 140	$ 249	$ 597	$ 993
Operating expenses	7,739	10,414	10,563	14,993
Net loss and comprehensive loss	(6,411)	(9,763)	(9,844)	(13,868)
Net loss attributable to Spero Therapeutics, Inc.	(5,876)	(9,169)	(9,836)	(13,862)
Net loss attributable to common shareholders of Spero Therapeutics, Inc.	(7,130)	(12,121)	(12,076)	(14,770)
Net loss per share attributable to common shareholders per share, basic and diluted	$ (21.60)	$ (36.21)	$ (36.02)	$ (1.59)
Weighted average shares outstanding, basic and diluted:	330,075	334,788	335,285	9,273,783

	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
Grant Revenue	$ —	$ —	$ —	$ 335
Operating expenses	8,417	8,080	7,914	9,145
Net loss and comprehensive loss	(8,430)	(8,096)	(7,918)	(8,197)
Net loss attributable to Spero Therapeutics, Inc.	(5,905)	(6,059)	(6,316)	(7,211)
Net loss attributable to common shareholders of Spero Therapeutics, Inc.	(6,257)	(7,928)	(7,410)	(8,333)
Net loss per share attributable to common shareholders per share, basic and diluted	$ (21.51)	$ (25.30)	$ (23.23)	$ (25.68)
Weighted average shares outstanding, basic and diluted:	290,884	313,414	318,948	324,521

18. Subsequent Events

On January 17, 2018, the Company entered into an amendment to the lease agreement with respect to its corporate headquarters located at 675 Massachusetts Avenue, Cambridge, Massachusetts. The Amendment makes certain changes to the original lease, by and between the Company and U.S. REIF Central Plaza Massachusetts, LLC (the "Landlord"), including (i) the addition of approximately 7,800 square feet of office space in the same building (the "Expansion Premises") and (ii) an extension of the expiration date of the Original Lease to seven years following the delivery date of the Expansion Premises (the "Lease Term"), which is estimated to be December 1, 2018.

Under the 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. The Amendment provides for annual base rent for the Expansion Premises of approximately $0.5 million in the first year of the Lease Term, which increases on an annual basis to approximately $0.6 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.

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, 2017. 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, 2017, 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

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public 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, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Management and Corporate Governance Matters," "Section 16(a) Beneficial Ownership Reporting Compliance," and "Code of Conduct and Ethics" in the Company's proxy statement for the 2018 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 11. Executive Compensation.

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Executive Officer and Director Compensation," "Management and Corporate Governance Matters - Compensation Committee Interlocks and Insider Participation," "Compensation Committee Report" and "Compensation Practices and Policies Relating to Risk Management" in the Company's proxy statement for the 2018 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" in the Company's proxy statement for the 2018 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Certain Relationships and Related Transactions" and "Management and Corporate Governance Matters" in the Company's proxy statement for the 2018 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 14. Principal Accounting Fees and Services.

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Independent Public Accountants" in the Company's proxy statement for the 2018 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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 3.1)	11/6/2017	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
10.1#	2017 Stock Incentive Plan, as amended		Form 10-Q (Exhibit 10.1)	12/14/2017	333-220858
10.2#	Form of Stock Option Agreement under the 2017 Stock Incentive Plan, as amended		Form 10-Q (Exhibit 10.2)	12/14/2017	333-220858
10.3#	Form of Director and Officer Indemnification Agreement		Form S-1 (Exhibit 10.4)	10/6/2017	333-220858
10.4#	Non-Employee Director Compensation Policy		Form S-1/A (Exhibit 10.20)	10/23/2017	333-220858
10.5#	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
10.6#	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
10.7#	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
10.8#	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
10.9#	Employment Agreement, dated December 13, 2017, by and between the Registrant and David Melnick, M.D.	X			
10.10#	Letter Agreement, dated June 24, 2015, by and between the Registrant and John Tomayko, M.D.		Form S-1 (Exhibit 10.9)	10/6/2017	333-220858

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
10.11#	Termination and Release, dated April 14, 2017, by and between the Registrant and John Tomayko, M.D.		Form S-1 (Exhibit 10.10)	10/6/2017	333-220858
10.12	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
10.13	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
10.14	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
10.15†	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
10.16†	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
10.17†	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
10.18†	Amended and Restated License Agreement, dated June 28, 2017, by and between Spero Potentiator, Inc. and Northern Antibiotics Oy (Ltd.)		Form S-1/A (Exhibit 10.16)	10/23/2017	333-220858
10.19	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 10.15)	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			

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
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.

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, as amended, the registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

SPERO THERAPEUTICS, INC.

Date: April 2, 2018

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 Joel Sendek 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, as amended, 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)*	April 2, 2018
/s/ Joel Sendek Joel Sendek	Chief Financial Officer and Treasurer *(Principal Financial Officer and Principal Accounting Officer)*	April 2, 2018
/s/ Casper Breum Casper Breum	Director	April 2, 2018
/s/ Milind Deshpande, Ph.D. Milind Deshpande, Ph.D.	Director	April 2, 2018
/s/ Jean-François Formela, M.D. Jean-François Formela, M.D.	Director	April 2, 2018
/s/ David P. Southwell David P. Southwell	Director	April 2, 2018
/s/ Frank E. Thomas Frank E. Thomas	Director	April 2, 2018
/s/ Patrick Vinik, M.D. Patrick Vinik, M.D.	Director	April 2, 2018

Exhibit 10.9

EXECUTIVE EMPLOYMENT AGREEMENT

This Executive Employment Agreement (this "Agreement") is made and entered into this 13th day of December, 2017 (the "Effective Date") by and between Spero Therapeutics, Inc., a Delaware corporation ("Company"), and David A. Melnick ("Executive").

WHEREAS, Executive and Company desire to set forth the terms and conditions for the employment of the Executive by the Company to assure the harmonious performance of the affairs of Company as well as to enter into a Proprietary Information and Inventions Assignment Agreement (the "Restrictive Covenant Agreement").

NOW, THEREFORE, in consideration of the mutual promises, terms, provisions, and conditions contained herein, Company and Executive hereby agree as follows:

1. Roles and Duties. Subject to the terms and conditions of this Agreement, Company shall employ Executive as its Chief Medical 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 Medical 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 commence on January 4, 2018 (the "Start Date") and 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 are 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. Commencing on the Start Date Company shall pay Executive a base salary (the "Base Salary") at the annual rate of Three Hundred Eighty Thousand Dollars ($380,000). 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. Commencing with fiscal 2018, 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 thirty-five percent (35%) 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. On the Start Date, the Company shall award Executive a stock option under its 2017 Stock Incentive Plan (the "Plan") to purchase 135,000 shares of the Company's common stock at a per share exercise price equal to the fair market value (as defined in the Plan) of the Company's common stock on such date (the "Option"). The Option will be evidenced in writing by, and subject to the terms of, the Company's standard form of stock option agreement, which agreement will specify vesting over four (4) years, 25% on the first anniversary of the Start Date with the balance to vest in equal monthly installments over the following 36 months and exercise of vested options for up to ten (10) years except as otherwise provided in the stock option agreement or by the Plan. Commencing in fiscal year 2019, 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) Relocation Expenses. For the 2018 calendar year, Company shall reimburse Executive for or will pay on Executive's behalf reasonable relocation expenses for Executive's relocation to the Boston area, provided such expenses do not exceed $20,000 (the "Relocation Expenses"). Executive will submit all such Relocation Expenses for approval in accordance with Company's expense reimbursement policy. The amounts paid to or on behalf of Executive under this Section will be deemed imputed additional income to Executive to the extent required by law. In the event that Executive's employment hereunder is terminated by Executive for any reason prior to the one (1) year anniversary of the Start Date, Executive shall repay Company the amount of Relocation Expenses within fifteen (15) days of Executive's termination date. You hereby agree that any repayment of Relocation Expenses may be deducted from payments to be made by the Company upon termination, including from the Accrued Obligations.

(i) Sign-On Bonus. Company shall pay Executive a sign-on bonus (the) in the amount of Ten Thousand Dollars ($10,000) "Sign-On Bonus"), on the first payroll date following the Start Date provided that in the event that Executive resigns Executive's employment with Company without Good Reason or the Company terminates Executive for Cause within one (1) year following the Start Date, Executive shall repay Company the amount of the Sign-On Bonus

within fifteen (15) days of Executive's termination date. Company shall deduct from the Sign-On Bonus all amounts required to be deducted or withheld under applicable law or under any employee benefit plan in which Executive participates. You hereby agree that any repayment of the Sign-On Bonus may be deducted from payments to be made by the Company upon termination, including from the Accrued Obligations.

(j) 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. (A) All of Executive's unvested equity awards will accelerate and vest immediately on the date of termination of Executive's employment if such employment commenced at least twenty-four (24) months prior to a Change of Control, (B) 50% of Executive's unvested equity awards will vest immediately on the date of termination of Executive's employment if such employment commenced fewer than twenty-four (24) months but at least twelve (12) months prior to a Change of Control, and (C) 25% of Executive's unvested equity awards will vest immediately on the date of termination of Executive's employment if such employment commenced fewer than twelve (12) months prior to a Change of Control.

(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. In light of the foregoing acknowledgements, and as a condition of employment hereunder, Executive hereby approves the Restrictive Covenant Agreement entered into on the date hereof as a binding obligation of the Executive, enforceable in accordance with its terms.

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.

DAVID A. MELNICK

/s/ David A. Melnick
Signature

SPERO THERAPEUTICS, INC.

By: /s/Ankit Mahadevia, MD
Name: Ankit Mahadevia, MD
Title: President and CEO

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 Gyrase, Inc.	Delaware
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 Statement on Form S-8 (No. 333- 222060) of Spero Therapeutics, Inc. of our report dated April 2, 2018 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
April 2, 2018

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)) for the registrant and have:

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

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

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

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrants 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: April 2, 2018

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, Joel Sendek, 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)) for the registrant and have:

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

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

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

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

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

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

Date: April 2, 2018

By: /s/ Joel Sendek
Joel Sendek
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, 2017, 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: April 2, 2018

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, 2017, 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: April 2, 2018

By: /s/ Joel Sendek
Joel Sendek
Chief Financial Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer)