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, 2018

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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). YES ☒ NO ☐

Indicate by check mark 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	☐	Smaller reporting company	☒
		Emerging growth company	☒

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

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

The aggregate market value of Common Stock held by non-affiliates of the registrant computed by reference to the price of the registrant's Common Stock as of June 29, 2018, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $210.9 million (based on the last reported sale price on the Nasdaq Global Market as of such date). As of March 8, 2019, there were 17,215,976 shares of the registrant's 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 2019 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2018. 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.

Table of Contents

PART I

Forward-Looking Information

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

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

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

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

Item 1. Business.

Overview

We are a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing and commercializing novel treatments for multi-drug resistant, or MDR, bacterial infections. Our most advanced product candidate, SPR994 (also called tebipenem pivoxil hydrobromide), 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, which includes two intravenous, or IV-administered agents, SPR206 and SPR741, that are active either alone or in combination with other standard of care agents and are designed to treat MDR Gram-negative bacteria in the hospital. In addition, we are developing SPR720, an oral antibiotic designed for the treatment of a rare, orphan disease called pulmonary non-tuberculous mycobacterial infection, or NTM infection. 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, highlight the critical need for novel therapies, and in particular orally administrable agents, that are capable of overcoming these obstacles to effective patient treatment.

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

- ***Oral SPR994:*** ***Novel Antibiotic with Potential to be the First Broad-Spectrum Oral Carbapenem for Use in Adults.*** SPR994, also called tebipenem pivoxil hydrobromide, is our novel oral formulation of tebipenem, a carbapenem-class antibiotic marketed by Meiji Seika Pharma Co. Ltd., or Meiji, in Japan as Orapenem since 2009 for common pediatric infections. Carbapenems are an important class of antibiotics because they are safe and effective against drug-resistant Gram-negative bacterial infections. Carbapenem use has increased dramatically as a result of the rising resistance to commonly used agents such as fluoroquinolones and cephalosporin antibiotics. Carbapenems are now considered as the standard-of-care for treating these resistant bacteria, but they are currently only available intravenously for such indications. In September 2018, we announced positive results from the final analysis of our single ascending dose, or SAD, and multiple ascending dose, or MAD, Phase 1 clinical trial of SPR994 in healthy volunteers. Based on discussion from our pre-Phase 3 meeting with the U.S. Food and Drug Administration, or FDA, and positive results from the final analysis of our completed Phase 1 clinical trial of SPR994, we believe that positive results from a single pivotal Phase 3 clinical trial of SPR994 in complicated urinary tract infections, or cUTI, demonstrating a 10% non-inferiority margin would support the approval of SPR994 for the treatment of cUTI. In February 2019, we received FDA acceptance of our Investigational New Drug, or IND, application for SPR994 in cUTI. We intend to advance SPR994 at a dose of 600 mg administered three times per day, or TID, into a single pivotal Phase 3 clinical trial, called ADAPT-PO, in patients with cUTI. We have begun start-up activities for the ADAPT-PO clinical trial and anticipate opening trial sites around the end of March 2019 to support study enrollment. In addition to cUTI, we believe that SPR994 has the potential to treat other serious and life-threatening infections, including community acquired bacterial pneumonia, or CABP, for which we could receive funding support from the Biomedical Advanced Research and Development Authority, or BARDA, subject to BARDA exercising future options under our BARDA award, as further described in this section.

  Prior Safety and Efficacy Experience with Tebipenem Pivoxil in Japan

  Our clinical strategy is supported by extensive safety data underlying tebipenem pivoxil's regulatory approval in Japan and long-standing use in Japan for common pediatric infections. Approximately 1,200 subjects, including approximately 741 adults, have been dosed with tebipenem pivoxil at a range of doses in clinical and pharmacologic studies. In addition, Meiji has completed a post-market study including 3,540 patients following the safety and tolerability of tebipenem pivoxil at the approved dose. In addition, two exploratory Phase 2 trials were conducted in Japan in patients with cUTI, the first indication in which we intend to study for SPR994. We have the rights to all the registration and post-marketing studies.

  In addition, we 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. The QIDP designation was created by the Generating Antibiotic Incentives Now, or GAIN, Act and creates incentives for the development of certain antibiotics that treat serious or life-threatening infections. QIDP designation entitles us to priority review of 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 us global protection for SPR994, including in the United States and Europe, through 2038.

- ***IV Potentiator Platform (SPR206 and SPR741): Our Technology Designed to Treat Infections Caused by MDR Gram-Negative Bacteria in the Hospital Setting.*** Our Potentiator Platform is our novel and proprietary technology that we believe will enable us to develop drugs against MDR Gram-negative bacteria, a subset of bacterial organisms distinguished by the presence of an outer cell membrane. Our IV Potentiator Platform molecules are designed to treat MDR Gram-negative bacterial infections through interactions with the bacteria's outer cell membrane either as a monotherapy or by co-administering our Potentiator molecules with currently approved antibiotics, potentially making the existing antibiotics more effective by clearing a path for them to enter and kill the bacteria.

  We have two IV Potentiator Platform product candidates, SPR206 and SPR741. SPR206 is a direct acting IV-administered agent that has demonstrated single-agent antibacterial activity in preclinical studies against MDR Gram-negative bacteria, including *Acinetobacter baumanii* and *Pseudomonas aeruginosa*. SPR741 is an IV-administered agent to be used in combination that has demonstrated *in vitro* the ability to expand the spectrum and increase the potency of a co-administered antibiotic. Both have demonstrated potency against Gram-negative bacteria, including organisms identified by the Centers for Disease Control and Prevention, or CDC, and the World Health Organization, or WHO, as urgent and serious threats to human health.

  SPR206

  We continue to progress the development of our direct acting Potentiator Platform molecules, exemplified by our product candidate SPR206. In preclinical studies, SPR206 showed activity as a single agent against MDR and extensively drug resistant, or XDR, bacterial strains, including isolates of *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and carbapenem-resistant Enterobacteriaceae in both *in vitro* and *in vivo* models of infection. We have completed a preclinical toxicology study of SPR206 in accordance with good laboratory practice, or GLP, requirements. Data from recent preclinical studies of SPR206 suggest a potency and safety profile for SPR206 that may be superior to SPR741, and we believe SPR206 may have a potentially faster path to pivotal clinical trials when compared with SPR741 because SPR206 is being developed as a single agent. In May 2018, we announced preclinical toxicology and efficacy data that we believe support advancing SPR206 into clinical development. In December 2018, we initiated a Phase 1 clinical trial of SPR206, designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects. We expect to receive top-line data from this trial in the second half of 2019. We were granted QIDP designation by the FDA for SPR206 in October 2018 for the treatment of cUTI and hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia, or HABP/VABP.

  We have multiple patent applications pending for SPR206 that we believe will provide SPR206 protection globally, including in the United States and Europe, through 2039.

  SPR741

  The first clinical trial of SPR741 was a double-blind, placebo-controlled, ascending dose, multi-cohort trial. The trial was conducted in two parts, a SAD and a MAD. The SAD part of the trial was a single ascending dose design, with subjects receiving one dose of SPR741. The MAD part was a multiple ascending dose design, with subjects receiving repeat dosing over a period of 14 days. In both study parts, sequential cohorts were exposed to increasing doses of SPR741.

  Generally, there were no dose-related or treatment-related trends in any of the safety and tolerability endpoints for SPR741 when administered as single doses up to and including 800 mg or multiple doses up to and including 600 mg every 8 hours for 14 days.

  Following the completion of our first clinical trial, 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 the tolerability and pharmacokinetics of SPR741 as a single dose in combination with some commonly used beta-lactam antibiotics, including cephalosporins (ceftazidime), monobactams (aztreonam) and beta-lactams/beta-lactamase inhibitors (piperacillin/tazobactam). In this Phase 1b drug-drug interaction study, we observed no impact on the tolerability or standalone pharmacokinetics of SPR741 or the beta-lactam drug when the two are dosed together as a single dose, supporting further development of SPR741 as a combination agent for the treatment of MDR Gram-negative infections.

We believe that our intellectual property portfolio for SPR741 will provide SPR741 protection globally, including in the United States and Europe, through 2039.

As previously disclosed, we expect to select either SPR741 or SPR206 to bring forward as our lead Potentiator Platform product candidate, based on our evaluation of available clinical data for each candidate and other factors, and we expect to seek partnering opportunities or other non-dilutive funding for further clinical development of the Potentiator Platform candidate we elect to deprioritize. In light of the positive data from our preclinical toxicology studies of SPR206, we initiated a Phase 1 clinical trial of SPR206 in December 2018 designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects. We expect top-line data from this trial in the second half of 2019. We expect that data from this Phase 1 clinical trial of SPR206, together with the data from our completed Phase 1b clinical trial of SPR741, will enable us to select a lead Potentiator Platform product candidate to advance into late-stage development. Our current view is that a prioritization decision can best be made after each of our Potentiator Platform candidates has achieved a similar clinical development stage. Until such time, we expect to continue to assess clinical development strategies, partnering opportunities and non-dilutive funding for both of our Potentiator Platform product candidates.

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

  In November 2018 we announced positive results from preclinical IND-enabling studies of SPR720. SPR720 was assessed in a series of non-clinical studies, including IND-enabling 28- and 31-day GLP toxicology studies in non-human primates and rats, respectively, and safety pharmacology studies. Results from *in vitro* minimum inhibitory concentration, or MIC, studies demonstrated potent activity for SPR720 against prevalent NTM pathogens, including *Mycobacterium avium* complex and *Mycobacterium abscessus*. Furthermore, *in vivo* studies in murine models of pneumonia demonstrated favorable efficacy relative to standard-of-care comparator agents. The data suggest that SPR720 has an acceptable safety profile, encouraging target pathogen efficacy, and a wide therapeutic margin. We believe these results, in conjunction with recent regulatory interactions, support the further development of SPR720. We initiated a Phase 1 clinical trial of SPR720 in January 2019, designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects, and expect top-line data from this trial in the second half of 2019. In February 2019, we received QIDP designation for SPR720 for the treatment of lung infections caused by nontuberculous mycobacteria and for the treatment of lung infections caused by *Mycobacterium tuberculosis*. QIDP designation entitles us to priority review of SPR720 for regulatory approval by the FDA. The QIDP designation for SPR720, however, does not guarantee a faster development process or ensure FDA approval.

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

Recent Developments

SPR994 Phase 1 Final Results and Dose Selection Data Supporting Planned Single Pivotal Phase 3 Clinical Trial

In September 2018, we announced positive results from the final analysis of our Phase 1 clinical trial of SPR994 in healthy volunteers. The final data support the advancement of SPR994 at a dose of 600 mg administered TID into our planned ADAPT-PO pivotal Phase 3 clinical trial. Following positive feedback from the FDA from our pre-Phase 3 meeting, we believe that positive results from a single pivotal Phase 3 clinical trial of SPR994 in cUTI demonstrating a 10% non-inferiority margin would support the approval of SPR994 for the treatment of cUTI. As a result of the meeting, we submitted an IND application for SPR994 in cUTI with the FDA,

and in February 2019 we received FDA acceptance of our IND application for SPR994 in cUTI. We have begun start-up activities for the ADAPT-PO clinical trial and anticipate opening trial sites around the end of March 2019 to support study enrollment.

SPR720 Preclinical Data Supports Advancement into Phase 1 Clinical Trials

In November 2018, we announced positive results from preclinical IND-enabling studies of SPR720, our oral antimicrobial agent being developed for the treatment of NTM infections. SPR720 was assessed in a series of non-clinical studies, including IND-enabling 28- and 31-day GLP toxicology studies in non-human primates and rats, respectively, and safety pharmacology studies. Results from *in vitro* MIC studies demonstrated potent activity for SPR720 against prevalent NTM pathogens, including *Mycobacterium avium* complex and *Mycobacterium abscessus*. Furthermore, *in vivo* studies in murine models of pneumonia demonstrated favorable efficacy relative to standard-of-care comparator agents. The data suggest that SPR720 has an acceptable safety profile, encouraging target pathogen efficacy, and a wide therapeutic margin. We believe these results, in conjunction with recent regulatory interactions, support the further development of SPR720. In January 2019, we initiated a Phase 1 clinical trial of SPR720 in January 2019, designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects. We expect to receive top-line data from this trial in the second half of 2019. In addition, in February 2019, we received QIDP designation for SPR720 for the treatment of lung infections caused by nontuberculous mycobacteria and for the treatment of lung infections caused by *Mycobacterium tuberculosis*. QIDP designation entitles us to priority review of SPR720 for regulatory approval by the FDA. The QIDP designation for SPR720, however, does not guarantee a faster development process or ensure FDA approval.

SPR206 License Agreement with Everest Medicines

On January 4, 2019, the Company, through our wholly owned subsidiary New Pharma License Holdings Limited, or NPLH, entered into a license agreement with Everest Medicines II Limited, or Everest, whereby we granted Everest an exclusive license to develop, manufacture and commercialize SPR206, or products containing SPR206, in Greater China, South Korea and certain Southeast Asian countries. We retained development, manufacturing and commercialization rights with respect to SPR206 and Licensed Products in the rest of the world and also retained the right to develop or manufacture SPR206 and Licensed Products in the Territory for use outside the Territory. In addition to the license grant with respect to SPR206, we also granted to Everest a 12-month exclusive option to negotiate with us for an exclusive license to develop, manufacture or commercialize SPR741 in the same territories. We received from Everest an upfront payment of $3.0 million and are eligible to receive milestone payments of up to an additional $59.5 million upon Everest's achievement of specified clinical, regulatory and commercial milestones related to SPR206, of which we anticipate receiving at least $2.0 million in near-term milestones during 2019. Furthermore, we are eligible to receive high single-digit to low double-digit royalties on net sales of products containing SPR206 in the covered territories following regulatory approval of SPR206.

Our Pipeline

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

Our Strategy

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

- ***Advance our lead product candidate SPR994 through clinical development and regulatory approval.*** We initiated a Phase 1 dose-selection clinical trial of SPR994 in Australia in October 2017. In September 2018, we announced positive results from the final analysis of our Phase 1 clinical trial of SPR994 in healthy volunteers and identified a dose of 600 mg TID for our planned ADAPT-PO single pivotal Phase 3 clinical trial of SPR994 in cUTI. Our Phase 3 trial is designed to show that oral SPR994 is non-inferior to IV ertapenem and has a similar safety profile, supporting SPR994's value proposition of getting patients out of the hospital earlier or keeping them out of the hospital. In February 2019, we announced the FDA's acceptance of our IND application for SPR994 in cUTI. In addition to cUTI, we believe that SPR994 has the potential to treat other serious and life-threatening infections, including community acquired pneumonia, or CAP. In addition, our SPR994 collaboration with BARDA, which is further described elsewhere in this Business section, could provide funding for a possible clinical trial in pneumonia patients if BARDA elects to exercise its options under our BARDA award.
- ***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. We believe 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. We intend to continue to advance SPR720 through clinical development. In January 2019, we announced the initiation of a Phase 1 trial for SPR720 and expect to receive top-line data from this trial in the second half of 2019.
- ***Advance a product candidate from our IV Potentiator Platform through clinical development and regulatory approval, either through a collaboration or with non-dilutive funding (or both)***. In December 2018, we initiated a Phase 1 trial of SPR206 in healthy subjects. Data from recent preclinical studies of SPR206 suggest a potency and safety profile that may be superior to SPR741, and we believe SPR206 may have a potentially faster path to pivotal clinical trials compared with SPR741 because SPR206 is being developed as a single agent. We expect to decide which of these product candidates we will bring forward as our lead clinical Potentiator product candidate based on data from our ongoing Phase 1 clinical trial of SPR206, which we expect to receive in the second half of 2019, and data from our completed Phase 1 clinical trial of SPR741. We may seek partnering opportunities or other non-dilutive funding for further clinical development of the Potentiator candidate we elect to deprioritize.
- ***Maximize the value of our pipeline through collaborations with other pharmaceutical companies. We may elect to pursue strategic collaborations with other pharmaceutical companies to leverage our Potentiator Platform.*** We believe it may be beneficial to develop and commercialize one or more of our Potentiator product candidates through partnering opportunities. Such collaborations may include regional collaborations to advance the entire Potentiator Platform, or product-specific deals pairing our product candidates with collaborators' antibiotics, whether generic or novel, with the intention of enhancing those antibiotics' performance and efficacy. We believe this approach will facilitate the capital-efficient development and commercialization of our Potentiator Platform. As part of this strategy, in January 2019, we entered into a license agreement with Everest Medicines to develop, manufacture and commercialize SPR206 in Greater China, South Korea and certain Southeast Asian countries and granted Everest a 12-month exclusive option to negotiate with us for an exclusive license to develop, manufacture or commercialize SPR741 in the same territories.
- ***Continue to pursue collaborations with non-commercial organizations for scientific expertise and funding support.*** We have received funding support from BARDA, the U.S. National Institute of Allergy and Infectious Diseases, or NIAID, the U.S. Department of Defense, or DoD, and the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, a public-private partnership funded by BARDA within the U.S.

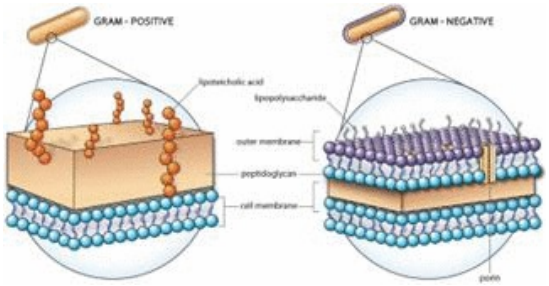
Department of Health and Human Services. We intend to continue to collaborate with government agencies and non-profit foundations to support the development of our product candidates.

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

The Problem: Increasingly Limited Antibiotic Options for Severe Infections

Antibiotic Background

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



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

Antibiotics are evaluated according to several criteria, including:

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

Growing Antibiotic Resistance in the Hospital and Community Settings

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

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

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

Chronic Bacterial Infection without a Viable Cure

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

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

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

Our Solution

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

- ***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***. Resistance to most commonly used classes of oral antibiotics, such as cephalosporins and fluoroquinolones, has increased significantly. Many of the most commonly used antibiotics for MDR Gram-negative infections are only available in an IV-administered formulation. Treatment with effective orally administrable antibiotics may prevent hospitalizations for serious infections and enable earlier, more convenient and cost-effective treatment of patients following hospitalization. SPR994 is an orally administrable tablet that we believe has the potential, if approved, to treat such infections in both the community and hospital settings, thereby preventing certain hospitalizations and enabling patients to transition to oral treatment. In the community setting, SPR994, if successfully developed and approved, may allow patients who develop an infection with a resistant pathogen, but are stable enough to be treated in the community, to avoid the need for an IV catheter

and even hospitalization. Hospitalization is a key cost driver for hospital systems and payers, with increasing emphasis being placed on hospital avoidance. In the hospital setting, the lack of effective oral stepdown options results in the potential for lengthy hospital stays or the insertion of a peripherally inserted central catheter, or PICC, to facilitate outpatient administration of IV antibiotics. SPR994 may enable faster discharges, providing cost-saving advantages for the hospital and mitigating the risk of catheter-related infection for patients.

- ***SPR206 and SPR741 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 IV empiric antibiotics, such as levofloxacin, ceftazidime and piperacillin-tazobactam, have experienced diminished utility as the number of bacterial strains resistant to these antibiotics in the hospital has increased. Due to gaps in the spectrum of coverage of antibiotics currently on the market, physicians are often confronted with the need to design complicated multi-drug cocktails for patients with serious infections. Based on results from preclinical studies to date, we believe that SPR206 has the potential to address this need as a single agent. 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.
- ***SPR720 is designed to be the first oral treatment for NTM infection where treatment failure is common and no approved therapies exist***. The current treatment for NTM infection is lengthy and involves combination therapy, often including three or more antibiotics, including injectables. None of these combination treatments are currently approved for use in NTM infection. Treatment failure is common and is often due to poor compliance or patients' inability to tolerate the regimen. Many patients experience progressive lung disease as a result of NTM infection, and mortality rates are high, ranging from 29% to 69% within five years of diagnosis. We believe SPR720, if successfully developed, has the potential to be the first approved oral agent for NTM infection, and it has demonstrated activity *in vitro* and *in vivo* against a range of pathogens, including *Mycobacterium abscessus*, a highly resistant organism causing NTM infection with a high rate of mortality.

Our Product Candidates

SPR994 (Tebipenem Pivoxil Hydrobromide)

Our lead product candidate, SPR994, also called tebipenem pivoxil hydrobromide, is a broad-spectrum oral carbapenem intended for use in adults to treat MDR Gram-negative infections. We have begun start-up activities for our planned ADAPT-PO pivotal Phase 3 clinical trial of SPR994 in cUTI and anticipate opening trial sites around the end of March 2019 to support study enrollment. Carbapenems have been utilized for over 30 years and are considered the standard of care for many serious MDR Gram-negative bacterial infections, but to date they have only been available as IV-administered formulations. Currently, there are no commercially available oral carbapenems for use in adults, and we believe SPR994 has the potential to address this unmet need. SPR994 is an oral tablet formulation of tebipenem. Tebipenem was approved in 2009 in Japan for sale under the name Orapenem for pediatric use in common infections. To accelerate our clinical development of SPR994, in June 2017 we signed an exclusive license to certain data and know-how from Meiji and a global pharmaceutical company, to which we refer as Global Pharma, which we intend to use to support our clinical development of SPR994. We have global commercialization rights to SPR994, except in certain contractually specified Asian countries.

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. 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 Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, for a total of 10 years. In Europe, exclusivity for NCEs is 10 years (eight years for data exclusivity and an additional two years for market exclusivity), with the possibility of a one-year extension if the chemical entity is approved for use in an additional indication. Additionally, we believe that our intellectual property portfolio for SPR994, which includes multiple patent applications pending, will provide SPR994 protection globally, including in the United States and Europe, through 2039.

Advantages of SPR994

Key attributes of SPR994 support our confidence in our plan to conduct a single pivotal Phase 3 clinical trial of SPR994 and in SPR994's commercial potential, if SPR994 receives regulatory approval. We believe SPR994 has the potential to be 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, if approved***. 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.

- ***Potential differentiated launch characteristics.*** There are limited branded or generic oral options currently approved or available to treat fluoroquinilone- and cephalosporin-resistant pathogens to assist with transitioning patients from the hospital to the community setting, or to prevent unnecessary hospitalization for cUTI. We believe SPR994, if approved, to be primarily reimbursable outside the hospital diagnosis-related group, or DRG, system, because of the limited number of doses required in the hospital setting. Together, we believe these factors could differentiate SPR994 from other recently launched antibiotic drugs, many of which are injectable, reimbursed within the hospital DRG system, and/or substitutable with equally effective generic alternatives.
- ***Single Phase 3 trial design supported by extensive clinical and preclinical studies.*** Spero's clinical and preclinical studies with SPR994 suggest that the safety, antimicrobial potency, and pharmacodynamics exposure profile observed to date are comparable to IV carbapenems. Data from our Phase 1 clinical trial of SPR994 studying a dosage of 600 mg three times per day (TID) have suggested a tolerability profile and pharmacodynamic activity in plasma and urine for SPR994 that are comparable to available data for IV-administered ertapenem given once daily. Data from Meiji's Phase 2 dose ranging study of tebipenem pivoxil in cUTI show microbiological eradication at test of cure comparable to other IV agents for cUTI. Also, the *in vitro* potency of SPR994 against Enterobacteriaceae was observed to be similar to IV-administered ertapenem and imipenem in preclinical studies. As a result of this extensive existing data, we believe that 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.
- ***Favorable safety, efficacy and tolerability profile suggested by clinical trials of tebipenem in Japanese populations***. A granule formulation of tebipenem has been approved for use in Japan in pediatric patients since 2009, where it has demonstrated a favorable safety and efficacy profile. Approximately 1,200 subjects have been dosed with the active pharmaceutical ingredient of SPR994, tebipenem, in clinical and pharmacologic studies during development of this drug by Meiji and its partner in Japan. This data set includes 741 adults, including 88 patients with cUTIs, the initial indication for which we are developing SPR994. In each case tebipenem has demonstrated a favorable safety, pharmacokinetic and tolerability profile. In addition, Meiji has conducted a 3,540 patient post-marketing study supporting the safety and tolerability profile of tebipenem, specifically demonstrating a safety profile that aligns well with that observed across the clinical trial program and tolerability in line with other broad spectrum oral antibiotics.
- ***Potential to enable IV-to-oral transition of antibiotic treatment to assist with reduction in hospital stays and/or eliminate the need for hospitalization.*** We believe the unique oral formulation of 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. 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:

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

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

IQVIA completed a market assessment in August 2017 in the community and hospital settings in which it estimated that there were 11 to 12 million patients annually who presented in the community physician's office with a UTI and 3.5 to 4.5 million patients annually in the hospital with a UTI in the United States alone. Of these UTIs, 10 to 11 million are suspected to be caused by Gram-negative bacteria, and 4 to 5 million of these patients had an infection that is resistant to or failed first-line therapy, such as the fluoroquinolone class, or require IV therapy due to the severity of infection. Physicians in the survey reported high concern with growing fluoroquinolone resistance and lack of oral options for MDR Gram-negative infections. We believe 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 planned pivotal Phase 3 clinical trial 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.

SPR994 Clinical Development Program

Planned Single Pivotal Phase 3 Clinical Trial (ADAPT-PO)

We initiated a Phase 1 dose-selection clinical trial of SPR994 in healthy volunteers in Australia in October 2017. In September 2018, we announced positive results from the final analysis of this study and identified a dose of 600 mg TID for our planned single pivotal Phase 3 clinical trial of SPR994 in cUTI. Based on our pre-IND, pre-Phase 3 meeting with the FDA, we believe that positive results from a single pivotal Phase 3 clinical trial of SPR994 in cUTI demonstrating a 10% non-inferiority margin would support the approval of SPR994 for the treatment of cUTI. As a result of the meeting, we submitted an IND application for SPR994 in cUTI with the FDA and received FDA acceptance of the IND application in February 2019. We have begun start-up activities for the ADAPT-PO clinical trial and anticipate opening trial sites around the end of March 2019 to support study enrollment. Following receipt of top-line data from our ADAPT-PO Phase 3 clinical trial of SPR994, if favorable, together 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.

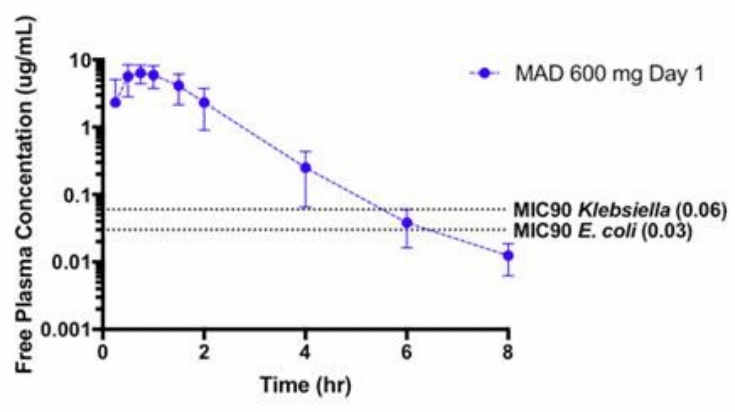
QIDP Designation

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 Hatch-Waxman Act.

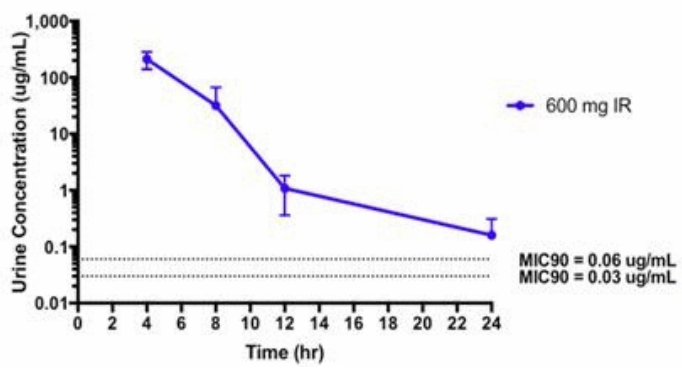
Phase 1 Clinical Trial Results

Our completed Phase 1 SAD and MAD clinical trial of SPR994 assessed the safety, tolerability and pharmacokinetics of orally administered SPR994. The Phase 1 clinical trial enrolled 124 healthy adult volunteers into 14 SAD cohorts with SPR994 given orally as single doses ranging from 100 mg to 900 mg daily and two MAD cohorts with SPR994 given orally at doses of 300 mg and 600 mg every 8 hours (TID administration) for 14 days. Repeated dose administration of both 300 mg and 600 mg of SPR994 TID was well tolerated, with a safety profile consistent with the carbapenem class of antibiotics. Final results demonstrated a linear and proportional increase in plasma exposure over the dose range tested, with no accumulation over 14 days of repeated dosing. Furthermore, the administration of SPR994 in the fed or fasting state did not substantially alter the plasma drug exposure, indicating that SPR994 can likely be administered without regard to meals. Consistent with the predominantly renal elimination of SPR994, peak urine concentrations were approximately 50 to 100-fold higher than maximum concentrations in plasma, as shown in the charts below, supporting SPR994's potential utility as a treatment for patients with cUTI.

Free Plasma Concentrations of SPR994



Urine Concentration of SPR994 after a Single Dose



The single planned pivotal Phase 3 clinical trial of SPR994, ADAPT-PO, is designed as a double-blind, double-dummy trial to compare oral SPR994 with an existing standard of care IV antibiotic, ertapenem, in approximately 1,200 patients randomized 1:1 in each arm. The primary endpoint of the pivotal trial will be the combined clinical and microbiological response at the test of cure with a 10% non-inferiority margin versus IV ertapenem. The trial will also incorporate a lead-in cohort of 70 patients with intensive pharmacokinetics assessment to confirm the dose and exposure in the cUTI patient population and we anticipate receiving interim pharmacokinetic and safety data from this lead-in cohort in the second half of 2019. We also plan to conduct routine ancillary clinical pharmacology studies in parallel with the Phase 3 trial as required by the FDA for the approval of SPR994, including a renal insufficiency study, a thorough QT prolongation study and a drug-drug interaction study.

In vitro Activity Against MDR Enterobacteriaceae

SPR994 has shown activity in preclinical *in vitro* studies against a wide variety of ESBL-producing *E. coli* and ESBL-producing K. pneumoniae strains. We believe these data show the ability of orally available SPR994 to deliver similar activity to comparative IV-administered agents.

Approximately 1,200 subjects have been dosed with tebipenem pivoxil in clinical and pharmacologic studies during the development of this drug by Meiji in Japan. The data set from these studies includes 741 adults, including 88 patients with cUTIs, the initial indication for which we plan to develop 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. We have also 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.

Meiji Phase 2 Clinical Trial Data of Tebipenem in cUTI

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

Although the design of the Phase 2 clinical trials in Japan was different from what is recommended in FDA guidance for clinical trials in patients with cUTI, including acute pyelonephritis, we believe these results provide support for our planned single pivotal Phase 3 clinical trial of SPR994 at a dose of 600 mg TID for the treatment of cUTI. With respect to these results, which are summarized in the chart below, the efficacy rate refers to the proportion of subjects judged to have experienced a “markedly effective” or “effective” tebipenem dosage versus the total number of subjects tested, and the negative conversion rate refers to the proportion of subjects with negative urine cultures versus the total number of subjects tested.

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

Study L-084 04

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

* Based on overall clinical outcome.

Study ME1211

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

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

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

*** "Markedly effective" or "effective."

In these two Phase 2 cUTI trials, 83-84% of patients had complicated lower tract UTIs (complicated cystitis). Taken together, the Meiji Phase 2 trials assessed the clinical and microbiological response to doses of tebipenem pivoxil ranging from 300 mg to 900 mg per day administered as two (BID) or three (TID) split doses. Clinical and microbiological responses at end of therapy, or EOT, were high for all regimens tested; however, the microbiological eradication rates at test of cure, or TOC, were highest in patients receiving tebipenem 150 mg or 300 mg TID. Of note, the microbiological eradication rates at the TOC in these dosing groups was similar to that reported for the subsets of patients with complicated cystitis in recent cUTI clinical trials utilizing intravenously administered antibiotics. Of note, the AUC exposure observed with 600 mg oral TID of SPR994 in the Spero single- and multiple-ascending dose study was comparable to that demonstrated to be effective in the Meiji cUTI trials. The appropriateness of the proposed therapeutic dose of SPR994 is supported by a pharmacokinetic/pharmacodynamic analysis based on three preclinical pharmacodynamic models (murine neutropenic thigh, hollow fiber, and one compartment pharmacodynamic model) and a clinical population pharmacokinetic model, which indicates that 600 mg of SPR994 administered TID is likely to achieve high target attainment over the MIC range of the most prevalent Enterobacteriaceae causing cUTI.

Japanese Data Supporting Safety of Tebipenem

Tebipenem pivoxil is a prodrug that is metabolized to tebipenem, its therapeutically active form. We view the clinical safety profile of tebipenem pivoxil established by Meiji as relevant and supportive of 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 1,200 subjects supporting the application for approval in Japan. In this safety data set, there are 741 adult subjects across 17 trials and 440 pediatric subjects across six trials. These 23 trials in total, included one double-blind, comparator-controlled trial in children, five open-label trials in children, five trials enrolling adult patients (including

two open-label cUTI trials), and 12 Phase 1 clinical pharmacology trials. Among the pharmacology trials, tebipenem pivoxil was studied for an effect on QT interval, and for the known effect of the pivoxil prodrug on plasma carnitine concentrations.

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

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

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

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

Funded Label Expansion Opportunity

In addition to cUTI, we believe that SPR994 has the potential to treat other serious and life-threatening infections, including CAP. Our BARDA award provides funding for Phase 1 and Phase 2 trials supporting a potential CAP indication for SPR994.

Our IV Potentiator Platform (SPR206 and SPR741)

We have two product candidates in our IV Potentiator Platform, SPR206 and SPR741, to treat Gram-negative infections in the hospital setting. Both have exhibited *in vitro* and *in vivo* activity against Gram-negative bacteria, including organisms identified by the CDC and the WHO as urgent and serious threats to human health. SPR206 has demonstrated antibacterial activity as a single agent and the ability to enhance the potency and spectrum of partner antibiotics. SPR206 demonstrates broad-spectrum MDR Gram-negative activity, including carbapenem-resistant *Pseudomonas aeruginosa*, carbapenem-resistant *Acinetobacter baumannii* and carbapenem-resistant Enterobacteriaceae. SPR741 has minimal observed antibacterial activity as a single agent and requires co-administration of a companion antibiotic to exert antimicrobial activity. SPR741 has demonstrated activity against MDR Gram-negative organisms, including carbapenem-resistant Enterobacteriaceae and carbapenem-resistant *Acinetobacter baumannii* depending on the combination partner.

In December 2018, we initiated a Phase 1 clinical trial of SPR206, designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects, and expect top-line data from this trial in the second half of 2019. Data from IND-enabling studies, together with data presented at the ESCMID/ASM Conference in September 2018, collectively demonstrate SPR206's favorable safety profile and *in vitro* activity against MDR Gram-negative pathogens.

We have completed a Phase 1, two-part, randomized, double blind, placebo-controlled, dose escalation trial of SPR741. The safety and pharmacokinetics data from this study were reported at the 2018 European Congress of Clinical Microbiology and Infectious Diseases, or ECCMID, congress in Madrid, Spain. The data 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 have also completed a 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-lactam/beta-lactamase inhibitors (piperacillin/tazobactam). The trial was designed to assess the impact, if any, on the standalone safety and pharmacokinetics of SPR741 or the standalone safety and pharmacokinetics of the beta-lactam combination drug when the two are dosed together as a single dose. In this study, we observed no impact on the safety or pharmacokinetics of SPR741 or the beta-lactam drug when the two are dosed together as a single dose, supporting further development of SPR741 as a combination agent for the treatment of MDR infections.

We have multiple patent applications pending for SPR206 that we believe will provide SPR206 protection globally, including in the United States and Europe, through 2039. Additionally, 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 2039.

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 Gram-negative infections:

- ***Potential to Expand the Potency of Standard-of-Care Antibiotics***. We believe SPR206 and SPR741 and 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 generally safe and well tolerated in Phase 1 and Phase 1b studies***. Data from our Phase 1 SAD and MAD clinical trial of SPR741 demonstrate SPR741 was generally safe and 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, as well as in combination with beta-lactam antibiotics.
- ***SPR206 may 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 aeruginosa* and *Acinetobacter baumannii*. Data from SPR206 *in vitro* and *in vivo* GLP safety pharmacology and absorption, distribution, metabolism, and excretion, or ADME, studies and 14-day, two-species GLP toxicology studies provide support for an acceptable safety profile, which led to SPR206's designation as a clinical candidate and the initiation of a Phase 1 clinical trial in December 2018. 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 SPR206 and SPR741, 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 and can cause severe and often deadly infections. As such, there is an acute need for new drugs to treat MDR Gram-negative bacterial infections. 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 MDR Gram-negative bacteria.

Acinetobacter baumannii is an opportunistic bacterial pathogen primarily associated with hospital-acquired infections with between 50,000 to 80,000 infections recorded annually in the United States and with approximately 63% of isolates exhibiting multi-drug resistance. 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 (PMB) and tigecycline (TIG), both of which have significant and dose limiting safety and tolerability issues. SPR206 would provide a much-needed alternative for the treatment of these very serious infections.

Pseudomonas aeruginosa is one of the most common Gram-negative organisms in the hospital setting. Incidence ranges from 13% in UTIs to 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. 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.

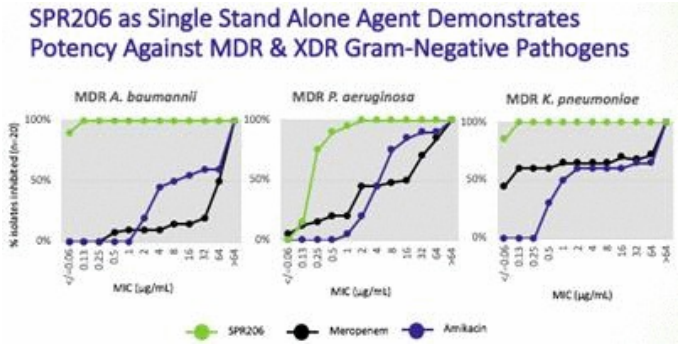
SPR206—Development Plan

Non-Clinical Data Supports the Progression of SPR206 to Clinical Development

SPR206 was assessed in a suite of non-clinical, IND-enabling studies, including 14-day, two species, GLP toxicology experiments and *in vitro* and *in vivo* GLP safety pharmacology and ADME studies. The data suggest the potential for an acceptable safety profile and add context to earlier microbiological and *in vivo* efficacy testing of SPR206 that demonstrated potent activity as a single agent against MDR and XDR bacterial strains, including carbapenem-resistant *Pseudomonas aeruginosa, Acinetobacter baumannii*, and Enterobacteriaceae. The composite data suggest SPR206 has the potential for wide therapeutic margins in the setting of serious hospital Gram-negative infections.

In Vitro Activity of SPR206 Against MDR Gram-Negative Bacteria

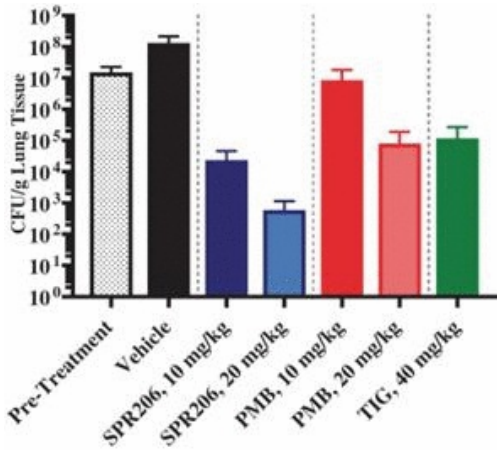
Results from multiple susceptibility testing studies against MDR Enterobacteriaceae suggests that SPR206 is capable potent activity against MDR Enterobacteriaceae, carbapenem resistant *Pseudomonas aeruginosa* and carbapenem resistant *Acinetobacter baumannii*.



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



Phase 1 Clinical Trial

In December 2018, we initiated a Phase 1 trial of SPR206, designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects. We anticipate receiving top-line data from the trial in the second half of 2019.

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.

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/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. In this study, we observed no impact on the tolerability or standalone pharmacokinetics of SPR741 or the beta-lactam drug when the two are dosed together as a single dose, supporting further development of SPR741 as a combination agent for the treatment of MDR infections.

Our Potentiator Platform product candidates (SPR206 and SPR741) are being funded in part with non-dilutive funding from the DoD, CARB-X and NIAID, consisting of $8.6 million through December 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, 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 these data demonstrate SPR741's ability to restore the combined antibiotic's therapeutic activity against a resistant strain of bacteria.

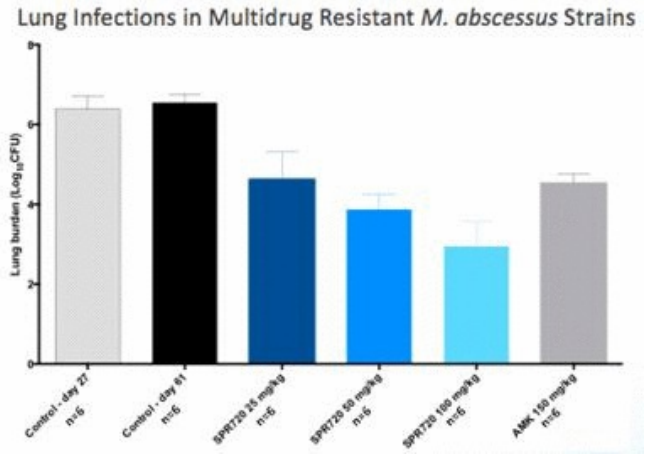
SPR720 Pulmonary Non-Tuberculous Mycobacterial (NTM) Infection Program

A third area of our focus is orphan infectious diseases, specifically non-tuberculous mycobacterial infection. We are developing SPR720, a therapeutic candidate with a novel mechanism of action for the treatment of NTM infection. SPR720 is designed to be the first novel, oral candidate to treat pulmonary NTM infection. SPR720 represents a novel class of antibacterial agents that target enzymes essential for bacterial DNA replication.

SPR720 has several key attributes including:

- ***Broad spectrum of activity.*** SPR720 has demonstrated a broad spectrum of activity against the most common organisms causing NTM infections, including *Mycobacterium avium* complex, or MAC, *Mycobacterium kansasii* and *Mycobacterium abscessus*.
- ***Convenient for patients.*** SPR720 is an oral antibiotic. Many patients can find inhalers difficult to use and poor inhalation technique can negatively impact drug delivery and response to therapy. Oral therapy is simple and more convenient.
- ***Novel mechanism.*** SPR720 employs a novel mechanism. Recent studies have shown the high prevalence of drug resistance in NTM infection species that threatens adequate control of the disease. Novel mechanisms may help evade existing modes of resistance.

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



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

NTM 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 and unfortunately, NTM infections are often undiagnosed, masquerading as another respiratory condition such as COPD or asthma. By comparison, the prevalence of tuberculosis in North America has declined.

There are currently no oral FDA-approved therapeutics specifically approved for use to treat pulmonary 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. Treatment of pulmonary NTM infections requires prolonged therapy (continuing for approximately 12 to 24 months) with a combination regimen and is frequently complicated by tolerability and/or toxicity issues. Treatment failure is common and is often due to poor compliance or inability to tolerate the regimen. Many patients experience progressive lung disease and mortality is high. We believe there is a need for new, potent, orally available therapies for NTM 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 clinical development. We assessed SPR720 in a series of non-clinical studies, including IND-enabling 28- and 31-day GLP toxicity studies in non-human primates and rats, respectively, and safety pharmacology studies. *In vitro* MIC studies demonstrated potent activity for SPR720 against prevalent NTM pathogens, including *Mycobacterium avium* complex and *Mycobacterium abscessus*. Furthermore, *in vivo* studies in murine models of pneumonia demonstrated favorable efficacy relative to standard-of-care comparator agents. The data suggest that SPR720 has an acceptable safety profile, encouraging target pathogen efficacy, and a wide therapeutic margin. These results, in conjunction with the recent regulatory interactions Spero has had, support the further development of SPR720. We initiated a Phase 1 clinical trial of SPR720 in January 2019, designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects, and expect top-line data from this trial in the second 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 developing. We have certain obligations under these acquisitions 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. In addition, we have entered into a license agreement (described below) pursuant to which we have granted certain development, manufacturing and commercialization rights with respect our Potentiator product candidates.

Meiji Agreements

To support our development of 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 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 ($6.4 million as of December 31, 2018) upon the achievement of a specified commercial milestone. We also agreed to pay royalties of a low single-digit percentage based on net sales of products licensed under the agreement. In addition, Spero Cantab issued an equity interest in Spero Cantab and entered into a subscription agreement and shareholders agreement with PBB. In July 2017, we repurchased PBB's minority equity interest in Spero Cantab in exchange for a one-time nonrefundable upfront fee of approximately $0.2 million and we also amended the Cantab Agreement to increase the contingent milestone payments to PBB by an aggregate of $0.1 million. The Cantab Agreement continues indefinitely, with royalty payment obligations thereunder continuing on a product-by-product and country-by-country basis until the later of ten years after the first commercial sale of such product in such country or the expiration in such country of the last to expire valid claim of any of the applicable patents. During the three months ended December 31, 2018, we recorded $0.2 million in expense related to the achievement of regulatory milestones for SPR206.

In addition, 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. Spero shall pay PBB a percentage of funds received from NIAID up to a maximum of $1.3 million, of which $0.3 million was paid upfront to PBB as part of this agreement. During the year ended December 31, 2018, we recorded approximately $0.4 million in expense related to amounts payable to PBB under this 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. During the three months ended December 31, 2018, we recorded $0.2 million in expense related to the achievement of regulatory milestones for SPR720. The agreement continues in effect until the expiration of all payment obligations thereunder, with royalty payment obligations continuing on a product-by-product and country-by-country basis until the later of ten years after the first commercial sale of such product in such country or the date of expiration in such country of the last to expire applicable patent. Further, Vertex has the right to terminate the agreement if provided with notification from us of our intent to cease all development or if no material development or commercialization efforts occur for a period of 12 consecutive months.

Everest Medicines License Agreement

On January 4, 2019, the Company, through its wholly owned subsidiary New Pharma License Holdings Limited, or NPLH, entered into a license agreement, or the Everest License Agreement, with Everest Medicines II Limited, which Everest License

Agreement also includes an option granted by our wholly owned subsidiary, Spero Potentiator, Inc., a Delaware corporation, or Potentiator. Under the terms of the License Agreement, we granted Everest an exclusive license to develop, manufacture and commercialize SPR206 or products that contain SPR206, or Licensed Products, in Greater China (which includes Mainland China, Hong Kong and Macau), South Korea and certain Southeast Asian countries, collectively referred to as the Territory. We retained development, manufacturing and commercialization rights with respect to SPR206 and Licensed Products in the rest of the world and also retained the right to develop or manufacture SPR206 and Licensed Products in the Territory for use outside the Territory. In addition to the license grant to SPR206, we granted Everest a 12-month exclusive option to negotiate with us for an exclusive license to develop, manufacture and commercialize SPR741 in the Territory.

Under the terms of the Everest License Agreement, we are entitled to receive an upfront payment of $3 million. We may also receive up to an additional $59.5 million in milestone payments upon Everest's achievement of certain developmental, regulatory and sales milestone events related to SPR206, which achievement cannot be guaranteed. We are also entitled to receive high single-digit to low double-digit royalties on net sales, if any, of Licensed Products in the Territory following regulatory approval of SPR206. Everest has the right to sublicense to affiliates and third parties in the Territory.

Everest is responsible for all costs related to developing, obtaining regulatory approval of and commercializing SPR994 and Licensed Products in the Territory, and is obligated to use commercially reasonable efforts to develop, manufacture and commercialize Licensed Products, including to achieve certain specified diligence milestones within agreed-upon periods. A joint development committee will be established between us and Everest to coordinate and review the development, manufacturing and commercialization plans with respect to Licensed Products in the Territory.

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

Government Awards

As described below, through December 31, 2018, we have committed funding support of up to an aggregate of $25.2 million in non- dilutive funding from BARDA, NIAID, the DoD and CARB-X, with the potential to receive a total of up to $54.3 million (inclusive of amounts we have already received) if certain options are exercised. These awards are structured in the following manner:

- BARDA award to support the further clinical development of SPR994. BARDA is providing initial funding of $15.7 million, with the potential for up to an additional $28.5 million over 5 years. The BARDA award commits funding of $15.7 million over a three-year base period from July 1, 2018 to June 30, 2021. The balance of the award is subject to BARDA exercising two options. As part of our SPR994 collaboration with BARDA described above, there will be studies assessing the efficacy of SPR994 in treatment of infections caused by biodefense threats such as anthrax, plague, and melioidosis, including a possible clinical trial in pneumonia patients. The Defense Threat Reduction Agency, or DTRA, will provide up to $10.0 million in addition to the total potential $44.2 million from BARDA, to cover the cost of the nonclinical biodefense aspects of the collaboration program. While such funding would be for the purpose of developing SPR994 in these areas, we will not receive any funds from DTRA. Upon these achievements, BARDA may exercise its second option to fund a bronchoalveolar lavage study to demonstrate safety and lung exposure sufficient to support efficacy and a clinical trial in pneumonia patients to demonstrate safety and data suggestive of efficacy.
- NIAID funding for SPR206. The NIAID contract for SPR206 provides for total development funding of up to $6.3 million over a base period and three option periods. To date, funding for the base period and the first two option periods, totaling $5.7 million, have been committed. The NIAID award is subject to termination for convenience at any time by NIAID, and NIAID is not obligated to provide funding to us beyond the base period amounts from Congressionally approved annual appropriations.
- NIAID award under its Small Business Innovation Research program, or SBIR for SPR720. This award provides up to $1.0 million of support for our SPR720 program. The scope of the program includes *in vitro* and *in vivo* assessments of SPR720 against tuberculous as well as nonclinical and manufacturing activities in support of both tuberculous and NTM indications. The NIAID SBIR award is structured as a base period followed by a single option. For the base period of March 1, 2017 through February 28, 2018, NIAID committed funding of approximately $0.6 million for the SPR720 program. In February 2018 NIAID exercised the approximately $0.4 million option, with a period of performance from March 1, 2018 through February 28, 2019. In January 2019, the period of performance for this award was extended for an additional 12-month period.

- Our Potentiator Platform program funding from DoD and CARB-X. The DoD funding supports next- generation Potentiator Platform discovery and screening of SPR741 partner antibiotics and SPR206. Our DoD cooperative agreement is structured as a single, two-year $1.5 million award. We are eligible for the full funding from the DoD and there are no options to be exercised at a later date. The CARB-X award supported 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. The CARB-X award was 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. In March 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.

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 – Tebipenem Pivoxil Hydrobromide)

Our SPR994 program contains one pending U.S. provisional application and two patent cooperation treaty, or PCT, applications covering novel preparations of tebipenem pivoxil hydrobromide as of December 31, 2018, all wholly owned by us. The provisional patent application must be converted to PCT applications within one year of its May 2018 filing date. U.S. and foreign patents issuing from our tebipenem pivoxil hydrobromide PCT 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, 2018, we owned or were exclusively licensed eight U.S. patents, two pending U.S. patent applications, and one U.S. provisional application; 100 foreign patents and ten 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. Issued U.S. or foreign patents and any patents issuing any pending U.S. or foreign applications covering SPR741 will have a statutory expiration date of August 2027, February 2029, April 2037, May 2037, and July 2039. Patent term adjustments or patent term extensions could result in later expiration dates.

Next-Generation Potentiator Platform Program (Including SPR206)

The intellectual property portfolio for our next-generation polymyxin program contains patent applications and issued patents directed to composition of matter for polymyxin-like compounds with different structural features, pharmaceutical compositions comprising the same, and methods of use for these novel compounds and compositions. As of December 31, 2018, we owned one U.S. patent, three pending U.S. applications, one U.S. provisional application, one foreign patent, and 31 pending foreign patent applications in a number of jurisdictions including Argentina, Australia, Brazil, Canada, China, the European Union, Hong Kong, Israel, Japan, South Korea, Mexico, Russia, Taiwan, and Venezuela. Issued U.S. or foreign patents and any patents issuing from pending U.S. or foreign, applications covering our next-generation polymyxin program will have a statutory expiration date of November 2032, May 2034, March 2035, November 2035, or June 2039. Patent term adjustments or patent term extensions could result in later expiration dates.

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, 2018, we owned eleven issued U.S. patents, 74 issued foreign patents, and 13 pending foreign patent applications. The issued and foreign patents are in a number of jurisdictions including the European Union and its member states, Argentina, Australia, Brazil, Canada, China, Hong Kong, Indonesia, Israel, India, Japan, South Korea, Mexico, New Zealand, the Philippines, Russia, Singapore, South Africa, and Taiwan. Issued U.S. and foreign patents, and patents issuing from pending U.S. and foreign applications will have statutory expiration dates of January 2032, June 2032 and July 2033. Patent term adjustments or patent term extensions could result in later expiration dates.

Patent Term and Patent Term Extensions

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

Trade Secrets

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

Competition

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

We believe the key competitive factors that will affect the development and commercial success of most advanced product candidate, 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 ceftibuten/clavulanate ("C-Scape") from Achaogen, Inc., sulopenem from Iterum Therapeutics Limited, 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 supported by years of post-marketing experience in Japan;
- a convenient oral dosing regimen and opportunity to step-down from IV-administered therapy; and
- as a monotherapy treatment for MDR Gram-negative infections.

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

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

Government Regulation and Product Approval

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

Recent Changes in the Regulatory Landscape

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

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

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an

approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil and/or criminal penalties.

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

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

Preclinical Studies

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

Clinical Trials

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

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

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

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

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

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

Marketing Approval

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

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

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

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

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

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

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

The FDA generally accepts data from foreign clinical trials in support of an NDA if the trials were conducted under an IND. If a foreign clinical trial is not conducted under an IND, the FDA nevertheless may accept the data in support of an NDA if the study was

conducted in accordance with GCPs and the FDA is able to validate the data through an on-site inspection, if deemed necessary. Although the FDA generally requests that marketing applications be supported by some data from domestic clinical trials, the FDA may accept foreign data as the sole basis for marketing approval if (1) the foreign data are applicable to the U.S. population and U.S. medical practice, (2) the studies were performed by clinical investigators with recognized competence, and (3) the data may be considered valid without the need for an on-site inspection or, if the FDA considers the inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

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

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

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

Special FDA Expedited Review and Approval Programs

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

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

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

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

verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

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

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

Post-Approval Requirements

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

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

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

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

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

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

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

- injunctions or the imposition of civil or criminal penalties.

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

Exclusivity and Approval of Competing Products

Hatch-Waxman Exclusivity

Market and data exclusivity provisions under the FDCA can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the activity of the drug substance. We believe that our product candidates are new chemical entities. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company that references the previously approved drug. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA, or supplement to an existing NDA or 505(b)(2) NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant, are deemed by the FDA to be essential to the approval of the application or supplement. Three-year exclusivity may be awarded for changes to a previously approved drug product, such as new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. For drug products that contain an "antibiotic" ingredient approved prior to 1997, the statute imposes certain limitations on the award of non-patent exclusivity. However, we do not believe these limitations would apply to 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. We were granted QIDP designation by the FDA for SPR206 in October 2018 for the treatment of cUTI and hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP). We were granted QIDP designation for SPR720 capsule for oral use for the treatment of lung infections caused by nontuberculous mycobacteria and for the treatment of lung infections caused by *Mycobacterium tuberculosis*.

Upon approving an application for a qualified infectious disease product, the FDA will extend by an additional five years any non-patent marketing exclusivity period awarded, such as a five-year exclusivity period awarded for a new molecular entity. 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, 2018, we had 41 full-time employees, including a total of 14 employees with M.D. or Ph.D. degrees. 25 employees were primarily engaged in research and development activities, with the rest providing administrative, business and operations support. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our employee relations to be good.

Our Corporate Information

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

Available Information

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

Item 1A. Risk Factors.

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

Risks Related to Our Financial Position and Need for Additional Capital

We have 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 $41.7 million, $39.9 million and $32.6 million for the years ended December 31, 2018, 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 sales of our equity securities, 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; and
- acquire or in-license other product candidates and technologies.

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

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

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

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete. We expect that our expenses will increase substantially as we commence and advance our ongoing and planned clinical trials and other studies of SPR994, SPR720 and SPR206, seek marketing approval for SPR994 if clinical trials are successful, and evaluate the advancement of our other product candidates. 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, cash equivalents and marketable securities as of December 31, 2018, together with the initial funding committed under our BARDA award in July 2018, will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2020, including through the top-line readout of our planned pivotal Phase 3 clinical trial of SPR994. Our cash forecasts are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the timing, costs and results of our ongoing and planned clinical trials of SPR994;
- the timing, costs and results of our ongoing, planned and potential clinical trials for other product candidates;
- the amount of funding that we receive under our government awards;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for 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, 2018, 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, an award from NIAID under its Small Business Innovation Research program or SBIR, for our SPR720 program, an award from NIAID for SPR206, and most recently, an award from BARDA for SPR994.

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 SBIR award is structured as a base period followed by a single option. For the base period of March 1, 2017 through February 28, 2018, NIAID committed funding of approximately $0.6 million for the SPR720 program. In February 2018 NIAID exercised the approximately $0.4 million option, which will have a period of performance from March 1, 2018 through February 28, 2019. In January 2019, the period of performance for this award was extended for an additional 12-month period. The NIAID contract for SPR206 provides for total development funding of up to $6.3 million over a base period and three option periods. To date, funding for the base period and the first two option periods totaling $5.7 million have been committed. The CARB-X award is structured as a base period followed by two sequential options. In March 2017, CARB-X committed funds of $1.5 million to support SPR741 development efforts for the period from April 1, 2017 to

March 31, 2018. On March 12, 2018, CARB-X committed an additional $0.4 million related to the first option for a period from December 1, 2017 to March 31, 2018. There will be no additional options exercised under the CARB-X award. The NIAID award is subject to termination for convenience at any time by NIAID. NIAID is not obligated to provide funding to Spero beyond the base period amounts from Congressionally approved annual appropriations.

The BARDA award commits funding of $15.7 million over a three-year base period from July 1, 2018 to June 30, 2021. The balance of the award is subject to BARDA exercising two options. As part of our SPR994 collaboration with BARDA described above, there will be studies assessing the efficacy of SPR994 in treatment of infections caused by biodefense threats such as anthrax, plague, and melioidosis, including a possible clinical trial in pneumonia patients. The nonclinical biodefense studies will be conducted by USAMRIID under the direction of the Company. DTRA will provide up to $10.0 million in addition to the total potential $44.2 million from BARDA, to cover the cost of the nonclinical biodefense aspects of the collaboration program. While such funding would be for the purpose of developing SPR994 in these areas, we will not receive any funds from DTRA. Upon these achievements, BARDA may exercise its second option to fund a bronchoalveolar lavage study to demonstrate safety and lung exposure sufficient to support efficacy and a clinical trial in pneumonia patients to demonstrate safety and data suggestive of efficacy.

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

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

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

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

As of December 31, 2018, we had U.S. federal, state and foreign net operating loss carryforwards, or NOLs, of $100.4 million, $100.3 million and $11.7 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.

Under recently enacted U.S. federal tax legislation, although the treatment of net operating loss carryforwards arising in tax years beginning on or before December 31, 2017 has generally not changed, net operating loss carryforwards arising in tax years

beginning after December 31, 2017 may be used to offset only 80% of taxable income. In addition, net operating losses arising in tax years beginning after December 31, 2017 may be carried forward indefinitely, as opposed to the 20-year carryforward under prior law.

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

We were established in 2013 and began operations in 2014. Our operations to date have been limited to financing and staffing our company, developing our technology and developing 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 clinical trials conducted by Meiji and a global pharmaceutical company, which we refer to as Global Pharma, in Japan, we may nonetheless fail to achieve success in our clinical trials. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates.

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

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

We may encounter unforeseen events prior to, during, or as a result of, clinical trials that could delay or prevent us from obtaining regulatory approval for 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 contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and 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 trial 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 its partner in Japan compared to the clinical trial design described by the FDA in its guidance for clinical trials in patients with cUTI, including:

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

If our planned pivotal Phase 3 clinical trial of SPR994 does not yield data that confirm the clinical and microbiological efficacy of SPR994 as suggested by the results from the Phase 2 clinical trials conducted by Meiji and its partner, then our clinical pathway for SPR994 could be delayed and our business could be materially harmed.

Preliminary or interim data from our clinical studies that we announce or publish from time to time, including preliminary data from our Phase 1 clinical trial of SPR994 and our dose-selection findings, may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

Preliminary or interim data from our clinical studies are not necessarily predictive of final data. Preliminary and interim data are subject to the risk that one or more of the clinical outcomes may materially change, as more patient data become available and we issue our final clinical study report. Preliminary or interim data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could affect our planned clinical path for SPR994, including potentially increasing cost and/or causing delay in such development.

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 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, SPR994 has generally been well tolerated in clinical trials conducted in healthy subjects and there have been no reports of serious adverse events related to SPR994, but additional adverse events may emerge in any subsequent clinical trials.

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

Undesirable side effects or other unexpected adverse events or properties of 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.

A Phase 2 clinical trial of SPR741 would be subject to a number of specific risks that may affect the outcome of the trial, 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.

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 urinary tract 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. However, the susceptibility of urinary tract pathogens to the existing treatment alternatives is waning. 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 ceftibuten/clavulanate ("C-Scape") from Achaogen, Inc., sulopenem from Iterum Therapeutics Limited, and omadacycline from Paratek Pharmaceuticals, Inc. If our competitors obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than us, it could result in our competitors establishing a strong market position before we are able to enter the market.

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

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

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

As a carbapenem, 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 our ongoing and planned clinical trials and potential approval of our lead product candidate, SPR994, our Potentiator Platform product candidates, SPR206 and SPR741, and SPR720, a key element of our strategy is to discover, develop and commercialize a portfolio of therapeutics to treat drug resistant bacterial infections. We are seeking to do so through our internal research programs and are exploring, and intend to explore in the future, strategic partnerships for the development of new product candidates.

Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- the research methodology used may not be successful in identifying potential product candidates;
- we may be unable to successfully modify candidate compounds to be active in Gram-negative bacteria or defeat bacterial resistance mechanisms or identify viable product candidates in our screening campaigns;

- competitors may develop alternatives that render our product candidates obsolete;
- product candidates that we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may, on further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors; and
- the development of bacterial resistance to potential product candidates may render them ineffective against target infections.

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

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

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we obtain marketing approval for and commercially sell 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, and could subject us to liability.

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

Despite the implementation of security measures, our internal computer systems and those of our contract research organizations and other contractors and consultants are vulnerable to damage or disruption from hacking, computer viruses, software bugs, unauthorized access, natural disasters, terrorism, war, and telecommunication, equipment and electrical failures. While we have not, to our knowledge, experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, 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.

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

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

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 it 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. For instance, in January 2019, we entered into a license agreement with Everest Medicines II Limited whereby we granted Everest an exclusive license to develop, manufacture and commercialize SPR206, or products containing SPR206, in Greater China, South Korea and certain Southeast Asian countries. In addition to the license grant with respect to SPR206, we also granted to Everest a 12-month exclusive option to negotiate with us for an exclusive license to develop, manufacture or commercialize SPR741 in the same territories. Our likely collaborators for any other marketing, distribution, development, licensing or broader collaboration arrangements we may pursue include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

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

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

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

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

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

We will require additional funds to complete the development and potential commercialization of 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. Moreover, we intend to utilize a variety of types of collaboration arrangements for the potential commercialization of our product candidates outside the United States. Whether we reach

a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include:

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

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

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

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

We do not independently conduct nonclinical studies that comply with GLP requirements. We also do not have the ability to independently conduct clinical trials of any of our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions, and clinical investigators, to conduct our clinical trials of SPR994 or our other product candidates and expect to rely on these third parties to conduct clinical trials of our other product candidates and potential product candidates. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities and increase our costs.

Our reliance on these third parties for clinical development activities limits our control over these activities but we remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example, notwithstanding the obligations of a contract research organization for a trial of one of our product candidates, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial and applicable regulatory requirements. While we will have agreements governing their activities, we control only certain aspects of their activities and have limited influence over their actual performance. The third parties with whom we contract for execution of our GLP studies and our clinical trials play a significant role in the conduct of these studies and trials and the subsequent collection and analysis of data. Although we rely on these third parties to conduct our GLP-compliant nonclinical studies and clinical trials, we remain responsible for ensuring that each of our nonclinical studies and clinical trials are conducted in accordance with applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities. The FDA and regulatory authorities in other jurisdictions also require us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to assure that data and reported results are accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. The FDA enforces these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable GCP standards,

the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the regulatory approval process. We cannot make assurances that, upon inspection, the FDA will determine that any of our clinical trials comply with GCP. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time and resources to our ongoing development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates. If that occurs, we may not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In such an event, our financial results and the commercial prospects for 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 our product candidates and expect to continue to do so in connection with any future commercialization and for any future clinical trials and commercialization of our other product candidates and potential product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently have nor do we plan to build the internal infrastructure or capability to manufacture 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. The inability or failure of our manufacturers to

successfully manufacture material that conforms to the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, may require us to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate. In addition, our manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and have a material adverse effect on our business, financial condition and results of operations.

Our current and anticipated future dependence upon others for the manufacture of 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.

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

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

We have received significant non-dilutive financing from various government agencies for the further development of our product candidates. Such funding sources may pose risks to us not encountered in other commercial contracts, including significant regulatory compliance risks. Contracts funded by the U.S. government and its agencies include provisions that reflect the government's substantial public policy and compliance requirements, and substantial rights and remedies, many of which are not typically found in commercial contracts, including powers of the government to:

- terminate agreements, in whole or in part, for any reason or no reason;
- reduce or modify the government's obligations under such agreements without the consent of the contractor;
- claim rights, including intellectual property rights, in products and data developed under such agreements;
- audit contract-related costs and fees, including allocated indirect costs;
- suspend the contractor from receiving new contracts pending resolution of alleged violations of procurement laws or regulations;

- impose U.S. manufacturing requirements for products that embody inventions conceived or first reduced to practice under such agreements;
- suspend or debar the contractor or grantee from doing future business with the government;
- control and potentially prohibit the export of products; and
- pursue criminal or civil remedies under the False Claims Act, or the FCA, the False Statements Act and similar remedy provisions specific to government agreements.

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

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

- specialized accounting systems unique to government awards;
- mandatory financial audits and potential liability for price adjustments or recoupment of government funds after such funds have been spent;
- public disclosures of certain award information, which may enable competitors to gain insights into our research program; and
- mandatory socioeconomic compliance requirements, including labor standards, anti-human-trafficking, non-discrimination and affirmative action programs, energy efficiency and environmental compliance requirements.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Certain of our activities have been funded, and may in the future be funded, by the U.S. government, including through our contracts with BARDA. When new technologies are developed with U.S. government funding, the government obtains certain rights in any resulting patents, including the right to a nonexclusive license authorizing the government to use the invention and rights that may permit the government to disclose our confidential information to third parties and to exercise "march-in" rights. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the U.S. government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal

regulations, or to give preference to U.S. industry. In addition, U.S. government-funded inventions must be reported to the government, U.S. government funding must be disclosed in any resulting patent applications, and our rights in such inventions may be subject to certain requirements to manufacture products in the United States.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient patent protection for our technology or our product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and product candidates may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary chemistry technology and product candidates. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and erode or negate any competitive advantage that we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we file patent applications in the United States and abroad related to our novel technologies and product candidates that are important to our business. The patent application and approval process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection.

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

Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

The laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, even assuming the other requirements for patentability are met, currently, in the United States, the first to make the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result of the America Invents Act of 2011, the United States transitioned to a first-inventor-to-file system in March 2013, under which, assuming the other requirements for patentability are met, the first inventor to file a patent application is entitled to the patent. However, as a result of the lag in the publication of patent applications following filing in the United States, we are still not be able to be certain upon filing that we are the first to file for patent protection for any invention. Moreover, we may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, *inter partes* review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may seek to market generic versions of any approved products by submitting Abbreviated New Drug Applications to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable and/or not infringed. Alternatively, our competitors may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid and/or unenforceable. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

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

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

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

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

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

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

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

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

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

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

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA or comparable foreign regulatory authority can subsequently approve the same drug for the same condition if such regulatory authority concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

If we are unable to obtain marketing approval in international jurisdictions, we will not be able to market our product candidates abroad.

In order to market and sell 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. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and puts into effect the migration from a "worldwide" system of taxation to a territorial system. As a result of the TCJA, our net deferred tax assets and liabilities existing as of December 31, 2017 were revalued at the newly enacted U.S. corporate rate. The impact of this tax reform is uncertain and could be adverse. We urge our investors to consult with their legal and tax advisors with respect to such legislation and the potential tax consequences of investing in our securities.

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

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

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

Risks Related to Employee Matters and Managing Growth

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

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

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

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

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

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

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

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

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;
- the perception of the pharmaceutical and biotechnology industry by the public, legislatures, regulators and the investment community;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;

- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to develop, in-license or acquire additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, 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.

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

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

The trading market for our common stock relies in part on the research and reports that securities or industry analysts publish about us or our business. If few analysts provide coverage of us, the trading price of our stock would likely 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 can issue and have issued shares of preferred stock, which may adversely affect the rights of holders of our common stock.

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

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

We have in the past issued, and we may at any time in the future issue, shares of preferred stock. In connection with our July 2018 public offering, we issued 2,220 shares of our Series A Convertible Preferred Stock to certain affiliates of Biotechnology Value Fund, L.P., or BVF, each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. In November 2018, we entered into an exchange agreement with BVF to exchange 1,000,000 shares of our common stock previously held by BVF for 1,000 shares of our Series B Convertible Preferred Stock, each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. If the holders of our shares of preferred stock convert their shares into common stock, existing holders of our common stock will experience dilution.

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

Our management will have broad discretion in the application of our cash reserves, including the proceeds from our IPO and our July 2018 equity offering, and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash reserves in a manner that does not produce income or that loses value.

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

We are an "emerging growth company," as defined in the 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 of 2002, or Sarbanes-Oxley, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and we will therefore be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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

As a public company, and particularly after we are no longer an "emerging growth company," we will incur significant legal, accounting and other expenses that we did not incur as a private company. Sarbanes-Oxley, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel 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. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

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

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

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Our outstanding shares of common stock may be freely sold in the public market at any time to the extent

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

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

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

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

As of December 31, 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 59% 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 15,600 square feet of office space. Our lease extends through December 2025. 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.

Holders of Record

On March 8, 2019, we had approximately 14 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, 2018, 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.

Use of Proceeds from Registered Securities

On November 6, 2017, we completed the initial public offering 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, 2018, we had used approximately $48.7 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, 2018, 2017, 2016 and 2015. We have derived the consolidated statement of operations data for the years ended December 31, 2018, 2017 and 2016, and the consolidated balance sheet data as of December 31, 2018 and 2017 from our audited consolidated financial statements included in this Annual Report on Form 10-K. We have derived the consolidated statement of operations data for the year ended December 31, 2015 and the consolidated balance sheet data as of December 31, 2016 and 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,			
	2018	2017	2016	2015
	(In thousands, except share and per share data)			
Consolidated Statement of Operations Data:				
Grant revenue	$ 3,966	$ 1,979	$ 335	$ —
Operating expenses:				
Research and development	33,885	32,869	26,333	11,125
General and administrative	12,887	10,840	7,223	2,202
Total operating expenses	46,772	43,709	33,556	13,327
Loss from operations	(42,806)	(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	1,144	303	—	—
Total other income (expense), net	1,144	1,844	580	174
Net loss	(41,662)	(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.	(41,662)	(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.	$ (41,662)	$ (46,097)	$ (29,928)	$ (13,427)
Net loss per share attributable to common stockholders of Spero Therapeutics, Inc. per share, basic and diluted(1)	$ (2.60)	$ (17.82)	$ (95.87)	$ (53.11)
Weighted average shares outstanding, basic and diluted(1):	16,001,832	2,586,865	312,169	252,807

	As of December 31,			
	2018	2017	2016	2015
			(in thousands)	
Consolidated Balance Sheet Data:				
Cash, cash equivalents and marketable securities	$ 115,443	$ 87,288	$ 10,315	$ 5,691
Working capital (deficit)	111,901	83,902	4,954	(433)
Total assets	129,006	93,749	13,772	7,176
Bridge units	—	—	7,924	—
Redeemable convertible preferred units	—	—	47,685	18,296
Total stockholders' equity (deficit)	115,855	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 (also called tebipenem pivoxil hydrobromide), 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, which includes two IV-administered agents, SPR206 and SPR741, that are active either alone or in combination with other standard of care agents and are designed to treat MDR Gram-negative bacteria in the hospital. In addition, we are developing SPR720, an oral antibiotic designed for the treatment of pulmonary NTM 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 our IPO 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.

On July 17, 2018, we completed an underwritten public offering of 3,780,000 shares of our common stock at a price of $12.50 per share, and 2,220 shares of our Series A Convertible Preferred Stock at a price of $12,500 per share. We received net proceeds from the offering of approximately $70.5 million after deducting underwriting discounts and commissions but before deducting $1.0 million of offering expenses payable by us.

On November 15, 2018, we entered into an Exchange Agreement, or the Exchange Agreement, with Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., Biotechnology Value Trading Fund OS, L.P. and MSI BVF SPV LLC (collectively, "BVF") pursuant to which BVF agreed to exchange an aggregate of 1,000,000 shares of our common stock, par value $0.001, owned by BVF for an aggregate of 1,000 shares of our newly designated Series B Convertible Preferred Stock, par value $0.001 per share, or the Series B Preferred Stock. On November 16, 2018, we designated 1,000 shares of our authorized and unissued preferred stock as Series B Convertible Preferred Stock.

Each share of the Series A and Series B Convertible Preferred Stock is convertible into 1,000 shares of our common stock at any time at the option of the holder, provided that the holder will be prohibited from converting the Series A and Series B Convertible Preferred Stock into shares of our common stock if, as a result of such conversion, the holder, together with its affiliates, would own more than 9.99% of the total number of shares of our common stock then issued and outstanding. In the event of our liquidation, dissolution, or winding up, holders of our Series A and Series B Convertible Preferred Stock will receive a payment equal to $0.001 per share of Series A and Series B Convertible Preferred Stock before any proceeds are distributed to the holders of our common stock. The Series A and Series B Convertible Preferred Stock have no voting rights, except as required by law and except that the consent of the Series A and Series B Convertible Preferred Stock holders will be required to amend the terms of the Series A Convertible Preferred Stock and the Series B Convertible Preferred Stock, respectively.

On December 3, 2018, we filed a universal shelf registration statement on Form S-3 (Registration No. 333-228661) with the SEC, which was declared effective on December 11, 2018, and pursuant to which we registered for sale up to $200.0 million of any combination of our common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on

terms that we may determine, including up to $50.0 million of our common stock available for issuance pursuant to an at-the-market offering program sales agreement that we entered into with Cantor Fitzgerald & Co., or Cantor. Under the sales agreement, Cantor may sell the shares by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415 of the Securities Act.

Prior to the IPO and our July 2018 equity offering, 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, 2018, we had an accumulated deficit of $138.5 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, 2018, we had cash, cash equivalents and marketable securities of $115.4 million. We believe that our existing cash, cash equivalents and marketable securities, together with the initial funding committed under our award with the Biomedical Advanced Research and Development Authority (BARDA) in July 2018, will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2020, including through top-line data readout of our planned pivotal Phase 3 clinical trial of SPR994. As described elsewhere, a portion of the funding from our BARDA award supporting the development of SPR994 is scheduled to occur in periods after 2020, provided we achieve specified milestones under the award agreement and BARDA exercises all of its options under the agreement.

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

SPR994 Phase 1 Final Results and Dose Selection Data Supporting Planned Single Pivotal Phase 3 Clinical Trial

In September 2018, we announced positive results from the final analysis of our Phase 1 clinical trial of SPR994 in healthy volunteers. The final data support the advancement of SPR994 at a dose of 600 mg administered TID into our ADAPT-PO pivotal Phase 3 clinical trial. Following positive feedback from the FDA from our Pre-Phase 3 meeting, we believe that positive results from a single pivotal Phase 3 clinical trial of SPR994 in cUTI demonstrating a 10% non-inferiority margin would support the approval of SPR994 for the treatment of cUTI. As a result of the meeting, we submitted an IND application for SPR994 in cUTI with the FDA, which was accepted by the FDA in February 2019. We have begun start-up activities for the ADAPT-PO clinical trial and anticipate opening trial sites around the end of March 2019 to support study enrollment.

The single planned pivotal Phase 3 clinical trial of SPR994, ADAPT-PO, is designed as a double-blind, double-dummy trial to compare oral SPR994 with an existing standard of care IV antibiotic, ertapenem, in approximately 1,200 patients randomized 1:1 in each arm. The primary endpoint of the pivotal trial will be the combined clinical and microbiological response at the test of cure with a 10% non-inferiority margin versus IV ertapenem. The trial will also incorporate a lead-in cohort of 70 patients with intensive pharmacokinetics assessment to confirm the dose and exposure in the cUTI patient population and we anticipate receiving interim pharmacokinetic and safety data from this lead-in cohort in the second half of 2019. We also plan to conduct routine ancillary clinical pharmacology studies in parallel with the Phase 3 trial as required by the FDA for the approval of SPR994, including a renal insufficiency study, a thorough QT prolongation study and a drug-drug interaction study.

SPR720 preclinical data supports advancement into Phase 1 clinical trials

In November 2018, we announced positive results from preclinical IND-enabling studies of SPR720, our oral antimicrobial agent being developed for the treatment of NTM infections. SPR720 was assessed in a series of non-clinical studies, including IND-enabling 28- and 31-day GLP toxicology studies in non-human primates and rats, respectively, and safety pharmacology studies. Results from *in vitro* MIC studies demonstrated potent activity for SPR720 against prevalent NTM pathogens, including *Mycobacterium avium* complex and *Mycobacterium abscessus*. Furthermore, *in vivo* studies in murine models of pneumonia demonstrated favorable efficacy relative to standard-of-care comparator agents. The data suggest that SPR720 has an acceptable safety profile, encouraging target pathogen efficacy, and a wide therapeutic margin. We believe these results, in conjunction with recent regulatory interactions, support the further development of SPR720. In January 2019, we initiated a Phase 1 clinical trial of SPR720, designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects. We expect to receive top-line data from this trial in the second half of 2019.

SPR206 license agreement with Everest Medicines

On January 4, 2019, the Company, through our wholly owned subsidiary NPLH, entered into a license agreement with Everest Medicines II Limited whereby we granted Everest an exclusive license to develop, manufacture and commercialize SPR206, or products containing SPR206, in Greater China, South Korea and certain Southeast Asian countries. We retained development, manufacturing and commercialization rights with respect to SPR206 and Licensed Products in the rest of the world and also retained the right to develop or manufacture SPR206 and Licensed Products in the Territory for use outside the Territory. In addition to the license grant with respect to SPR206, we also granted to Everest a 12-month exclusive option to negotiate with us for an exclusive license to develop, manufacture or commercialize SPR741 in the same territories. We received from Everest an upfront payment of $3.0 million and are eligible to receive milestone payments of up to an additional $59.5 million upon Everest's achievement of specified clinical, regulatory and commercial milestones related to SPR206, of which we anticipate receiving at least $2.0 million in near-term milestones during 2019. Furthermore, we are eligible to receive high single-digit to low double-digit royalties on net sales of products containing SPR206 in the covered territories following regulatory approval of SPR206.

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.

BARDA

In July 2018, we were awarded a contract from BARDA of up to $44.2 million to develop SPR994 for the treatment of cUTIs caused by antibiotic resistant Gram-negative bacteria and for assessment against biodefense pathogens. The award commits initial funding of $15.7 million over a three-year base period from July 1, 2018 to June 30, 2021 for cUTI development activities. The balance of the award is subject to BARDA exercising two options. The exercise of the first option would entail funding of $13.6 million and is exercisable by BARDA subject to our achieving specified milestones related to, among other things, clinical progress and data. The exercise of the second option would entail funding of $14.9 million and is exercisable by BARDA subject to, among other things, satisfactory progress and results from certain biodefense studies. We receive funding under the BARDA award as we incur qualifying expenses.

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 under its Small Business Innovation Research program 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. In January 2019, the period of performance for this award was extended for an additional 12-month period, through February 2020. 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 then CAI-held NIAID contract to us. Novation of the NIAID contract was finalized in December 2017. The NIAID contract provides for development funding of up to $6.3 million over a base period and three option periods. To date, funding for the base period and the first two option periods totaling $5.7 million have been committed. We will pay PBB a percentage of funds received from NIAID up to a maximum of $1.3 million of which $0.3 million was paid upfront to PBB as part of this agreement. During the year ended December 31, 2018, we recorded approximately $0.4 million in expense related to amounts payable to PBB under this agreement.

CARB-X

In April 2017, we received an award from the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, a public-private partnership funded by the BARDA 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. 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.

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 CROs;

- costs incurred in connection with our government awards;
- the cost of consultants and CMOs that manufacture drug products for use in our preclinical studies and clinical trials;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and supplies; and
- payments made under third-party licensing agreements.

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

Since the fourth quarter of 2016 and through December 31, 2018, we have recorded research and development expenses conducted by our Australian subsidiary net of a 43.5% research and development tax incentive we expect to receive for qualified expenses from the Australian government.

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,		
	2018	2017	$ Change
	(in thousands)		
Direct research and development expenses by program:			
SPR994	$ 11,412	$ 9,803	$ 1,609
Potentiator Platform (SPR206 and SPR741)	8,265	11,818	(3,553)
SPR720	2,579	1,585	994
Preclinical programs	—	1,337	(1,337)
Unallocated expenses:			
Personnel related (including share-based compensation)	8,027	5,724	2,303
Facility related and other	3,602	2,602	1,000
Total research and development expenses	$ 33,885	$ 32,869	$ 1,016

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 development activities in the near term and in the future as we progress our existing clinical trials and other studies of SPR994, SPR206 and SPR720, continue to discover and develop additional product candidates, hire additional clinical and scientific personnel and acquire or in-license other product candidates and technologies.

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

- successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- receipt of marketing approvals from applicable regulatory authorities;

- establishment of arrangements with third-party manufacturers to obtain manufacturing supply;
- obtainment and maintenance of patent, trade secret protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain our license agreement with Meiji with respect to 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, development, and commercialization 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, 2018, 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 primarily invested in money market accounts, as well as interest earned on our investments in marketable securities that we held during the year ended December 31, 2018. Other income (expense), net, consists of insignificant amounts of miscellaneous income, as well as realized and unrealized gains and losses from foreign currency-denominated cash balances, vendor payables and receivables from the Australian research and development tax incentive.

Income Taxes

Since our inception, we have not recorded any income tax benefits for the net losses we have incurred in each year or for our earned research and development tax credits, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating loss carryforwards and tax credits will not be realized. As of December 31, 2018, we had federal and state net operating loss carryforwards of $100.4 million and $100.3 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2033. In addition, as of December 31, 2018, we had foreign net operating loss carryforwards of $11.7 million, which may be available to offset future income tax liabilities and do not expire. As of December 31, 2018, we also had federal and state research and development tax credit carryforwards of $2.6 million and $0.8 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, 2018 and 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 BARDA, 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. We consider this revenue to be earned when we have substantially accomplished what we must do to be entitled to the benefits represented by the revenues. We record revenue from government contracts for qualifying expenses that we incur. 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 $1.2 million, $1.8 million and $0.1 million during the years ended December 31, 2018, 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 during the year ended December 31, 2016.

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. 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 Prior to our IPO

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 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, and 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.

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. 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, 2018, 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.

Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017:

	Year Ended December 31,		
	2018	2017	$ Change
	(in thousands)		
Grant revenue	$ 3,966	$ 1,979	$ 1,987
Operating expenses:			
Research and development	33,885	32,869	1,016
General and administrative	12,887	10,840	2,047
Total operating expenses	46,772	43,709	3,063
Loss from operations	(42,806)	(41,730)	(1,076)
Other income (expense):			
Change in fair value of derivative liabilities	—	1,541	(1,541)
Interest income and other income (expense), net	1,144	303	841
Total other income (expense), net	1,144	1,844	(700)
Net loss	(41,662)	(39,886)	(1,776)
Less: Net loss attributable to non-controlling interest	—	(1,143)	1,143
Net loss attributable to Spero Therapeutics, Inc.	$ (41,662)	$ (38,743)	$ (2,919)

Grant Revenue

	Year Ended December 31,		
	2018	2017	$ Change
	(in thousands)		
BARDA Contract (SPR994)	$ 1,373	$ —	$ 1,373
NIAID Contract (SPR206)	1,356	50	1,306
NIAID Award (SPR720)	490	383	107
DoD Agreement (Potentiator Platform)	282	674	(392)
CARB-X Award (SPR741)	465	872	(407)
Total grant revenue	$ 3,966	$ 1,979	$ 1,987

Grant revenue recognized during 2018 and 2017 consisted of the reimbursement of qualifying expenses incurred in connection with our various government awards. The increase in revenue during 2018 was primarily due to funding received under our BARDA contract, which was awarded to us in July 2018, and for which we began incurring qualified expenses in the second half of 2018, as well as the NIAID contract, which provides funding for SPR206, which was novated to us from CAI in December 2017. Offsetting these increases, were decreases in funding received under our DoD agreement, as well as our CARB-X award, which had a performance period through March 31, 2018.

Research and Development Expenses

	Year Ended December 31,		
	2018	2017	$ Change
	(in thousands)		
Direct research and development expenses by program:			
SPR994	$ 11,412	$ 9,803	$ 1,609
Potentiator Platform (SPR206 and SPR741)	8,265	11,818	(3,553)
SPR720	2,579	1,585	994
Preclinical programs	—	1,337	(1,337)
Unallocated expenses:			
Personnel related (including share-based compensation)	8,027	5,724	2,303
Facility related and other	3,602	2,602	1,000
Total research and development expenses	$ 33,885	$ 32,869	$ 1,016

Direct costs related to our SPR994 program increased during 2018 compared to 2017 primarily due to clinical trial costs, including expenses related to our Phase 1 clinical trial, which commenced in October 2017 and which was completed in August 2018, costs related to our pivotal Phase 3 clinical trial, as well as higher expenses related to formulation development, manufacturing process and manufacturing of clinical trial material. These increases were partially offset by a decrease in preclinical costs for this program related to costs incurred in 2017 in connection with the initiation our Phase 1 clinical trial, as well as $1.6 million of upfront and milestones payments incurred and paid in 2017 under our agreement with Meiji. Additionally, during 2018, research and development expenses for our SPR994 program conducted by our Australian subsidiary were recorded net of a 43.5% research and development tax incentive for qualified expenses from the Australian government of $0.9 million.

Direct costs related to our Potentiator Platform include costs related to our SPR206 and SPR741 programs. We designated SPR206 as a product candidate in July 2017, before which costs were captured as preclinical costs. Direct costs related to our SPR206 program increased by $6.0 million during 2018, primarily due to a full year of preclinical costs related to toxicology studies and manufacturing efforts to support our Phase 1 study of SPR206, which we initiated in December 2018, as well as $0.2 million in expense related to the achievement of regulatory milestones for SPR206. We expect direct costs related to our SPR206 program to continue to increase as we continue to progress our Phase 1 clinical trial. Direct costs related to our SPR741 program decreased by $9.5 million during 2018, primarily due to the completion of our Phase 1b drug-drug interaction clinical trial of SPR741 in the United Kingdom during the first half of 2018. Additionally, 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 less than $0.1 million in 2018, compared to $1.8 million in 2017. Because our Phase 1b clinical trial of SPR741 is complete, we anticipate that our direct costs related to our SPR741 program will continue at a reduced level pending our prioritization of our Potentiator product candidates.

Direct costs related to our SPR720 program increased during 2018 primarily related to costs incurred to prepare for the Phase 1 clinical trial of SPR720, which we initiated in January 2019, as well as related manufacturing expense and $0.2 million in expense related to the achievement of regulatory milestones for SPR720.

Direct costs related to our preclinical programs decreased by $1.3 million during 2018 compared to 2017 due primarily to lower spending on preclinical programs as we focused development efforts on our more advanced product candidates.

The increase in personnel-related costs of $2.3 million included in unallocated expenses was due to an increase in research and development headcount. Personnel-related costs for the twelve months ended December 31, 2018 and 2017 included share-based compensation expense of $1.1 million and $0.4 million, respectively. The increase in facility-related and other costs was primarily due to the increased costs of supporting a larger group of research and development personnel and their research efforts, as well as expense incurred during the third quarter of 2018, related to the write-off of certain leasehold improvements and laboratory equipment as a result of the closure of our Watertown, Massachusetts laboratory facility.

General and Administrative Expenses

	Year Ended December 31,		
	2018	2017	$ Change
		(in thousands)	
Personnel related (including share-based compensation)	$ 6,751	$ 4,330	$ 2,421
Professional and consultant fees	4,815	5,829	(1,014)
Facility related and other	1,321	681	640
Total general and administrative expenses	$ 12,887	$ 10,840	$ 2,047

The increase in personnel-related costs of $2.4 million was primarily a result of an increase in headcount in our general and administrative function as we operate as a public company. Personnel-related costs for the years ended December 31, 2018 and 2017 included share-based compensation expense of $1.7 million and $1.1 million, respectively.

The decrease in professional and consultant fees is primarily related to higher expenses incurred during 2017 in connection with the Reorganization as well as our preparations to operate as a public company.

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

Other Income (Expense), Net

Other income, net was $1.1 million during 2018, compared to $1.8 million during 2017. Other income, net for the year ended December 31, 2018 consisted of other income of $1.8 million, which was primarily related to interest income on our invested cash balances and marketable securities, partially offset by $0.7 million of other expenses. Other income, net was $1.8 million for the year ended December 31, 2017 and primarily consisted of 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, as well as interest income of $0.3 million related to interest earned on invested cash balances.

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	(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
Potentiator Platform (SPR206 and SPR741)	11,818	11,728	90
SPR720	1,585	1,181	404
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 by $1.3 million primarily due to a decrease in preclinical costs resulting from costs incurred in the prior year to support our Clinical Trial Notification, or 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 (a CTN, which is similar to an IND in the United States, enables conduct of a clinical trial in Australia). 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 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.

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.

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. 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.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We have generated limited revenue to date from funding arrangements with the DoD, NIAID, CARB-X and BARDA. 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, most recently, in November 2017 with proceeds from the IPO of our common stock, and in July 2018 with an underwritten public offering of our common and preferred stock. As of December 31, 2018, we had cash, cash equivalents and marketable securities of $115.4 million.

On December 3, 2018, we filed a universal shelf registration statement on Form S-3 (Registration No. 333-228661) with the SEC, which was declared effective on December 11, 2018, and pursuant to which we registered for sale up to $200.0 million of any combination of our common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that we may determine, including up to $50.0 million of our common stock available for issuance pursuant to an at-the-market offering program sales agreement that we entered into with Cantor Fitzgerald & Co. Under the sales agreement, Cantor may sell shares of our common stock by any method permitted by law deemed to be an “at the market” offering as defined in Rule 415 of the Securities Act, subject to the terms of the sales agreement. We have not sold any shares of our common stock under the sales agreement.

Cash Flows

The following table summarizes our sources and uses of cash for the years ended December 31, 2018, 2017 and 2016:

	Year Ended December 31,		
	2018	2017	2016
	(in thousands)		
Cash used in operating activities	$ (39,625)	$ (39,111)	$ (28,959)
Cash used in investing activities	(83,156)	(27)	(830)
Cash provided by financing activities	69,523	116,111	34,413
Net increase (decrease) in cash and cash equivalents	$ (53,258)	$ 76,973	$ 4,624

Operating Activities

Net cash used in operating activities for the year ended December 31, 2018 was $39.6 million, primarily resulting from our net loss of $41.7 million, adjusted for net non-cash items of $3.1 million. Net cash used by changes in our operating assets and liabilities was $1.1 million and consisted primarily of a $5.5 million increase in prepaid expenses and other current assets as we prepare to initiate our pivotal Phase 3 trial for SPR994, a $1.2 million increase in other assets, and partially offset by a decrease of $1.4 million in receivables related to the Australian research and development tax incentive and to our government contracts, and an increase in accounts payable and accrued expenses and other current liabilities of $3.7 million.

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.

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

Cash used in investing activities during the year ended December 31, 2018 was $83.2 million and primarily related to the net purchase of marketable securities, as well as $2.4 million of fixed assets purchased, which included $1.6 million of fixed assets which will be used in manufacturing related activities at Meiji. We did not use any significant cash for investing activities during the year ended December 31, 2017. During the year ended December 31, 2016, net cash used in investing activities was $0.8 million, consisting of purchases of property and equipment, primarily for our new office and laboratory spaces.

Financing Activities

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

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.

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;
- 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, cash equivalents and marketable securities, together with the initial funding committed under our BARDA award in July 2018, will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2020, including through the top-line data readout of our planned pivotal Phase 3 clinical trial of SPR994. However, we do not expect that these funds will be sufficient to fund the development of all of our product candidates through regulatory approval and commercialization. As described elsewhere, a portion of the funding from our BARDA award supporting the development of SPR994 is scheduled to occur in periods after 2020, provided we achieve specified milestones under the award agreement and BARDA exercises all of its options under the agreement.

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, 2018 and the effects that such obligations are expected to have on our liquidity and cash flows in future periods:

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

(1) Reflects payments due for our leases of laboratory and office space under operating lease agreements that expire in 2019 and 2025, respectively.

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, which was recorded as research and development expense in the statement of operations and comprehensive loss for the year ended December 31, 2017. Additionally, during the fourth quarter of 2018 we paid Meiji approximately $1.6 million related to fixed assets which will be used in manufacturing related activities at Meiji. The equipment has been capitalized as property and equipment in the consolidated balance sheet as of December 31, 2018.

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 ($6.4 million as of December 31, 2018) upon the achievement of a specified commercial milestone. In addition, we have agreed to pay to PBB royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement. During the three months ended December 31, 2018, we recorded $0.2 million in expense related to the achievement of regulatory milestones for SPR206.

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

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, and do not anticipate any such payments to be made in the future.

We enter into contracts in the normal course of business with CROs, CMOs and other third parties for clinical trials, preclinical research studies and testing, manufacturing and other services. These contracts are cancelable by us upon prior notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including non-cancellable obligations of our

service providers, up to the date of cancellation. These payments are not included in the table of contractual obligations and commitments above.

Off-Balance Sheet Arrangements

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

Recently Adopted Accounting Pronouncements

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

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

As of December 31, 2018, we had cash, cash equivalents and marketable securities of $115.4 million, consisting of cash, money market accounts, corporate bonds, commercial paper and U.S. government debt securities. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. If market interest rates were to increase immediately and uniformly by 50 basis points, from levels as of December 31, 2018, the net fair value of our interest sensitive marketable securities would hypothetically decline by approximately $0.1 million. As we incur research expenses in foreign countries, we face exposure to movements in foreign currency exchange rates, primarily the Euro, British Pound and Australian dollar against the U.S. dollar. Historically, foreign currency fluctuations have not had a material impact on our consolidated financial statements.

Item 8. Financial Statements and Supplementary Data.

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 (the "Company") as of December 31, 2018 and 2017, 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, 2018, 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, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018 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. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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

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
March 14, 2019

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,	
	2018	2017
Assets		
Current assets:		
Cash and cash equivalents	$ 34,080	$ 87,288
Marketable securities	81,363	—
Other receivables	376	1,011
Tax incentive receivable, current	922	1,932
Prepaid expenses and other current assets	7,478	1,828
Total current assets	124,219	92,059
Property and equipment, net	2,893	1,164
Deposits	153	206
Deferred offering costs	316	—
Other assets	1,192	—
Tax incentive receivable	233	—
Restricted cash	—	50
Total assets	$ 129,006	$ 93,479
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 3,603	$ 3,470
Accrued expenses and other current liabilities	8,263	4,321
Derivative liabilities	223	223
Deferred rent	229	143
Total current liabilities	12,318	8,157
Deferred rent, net of current portion	833	365
Total liabilities	13,151	8,522
Commitments and contingencies (Note 11)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized, 3,220 shares issued and outstanding as of December 31, 2018 and zero shares issued and outstanding as of December 31, 2017	—	—
Common stock, $0.001 par value; 60,000,000 shares authorized as of December 31, 2018 and December 31, 3017; 17,205,962 shares issued and outstanding as of December 31, 2018 and 14,369,182 shares issued and outstanding as of December 31, 2017	17	14
Additional paid-in capital	254,013	181,428
Accumulated deficit	(138,502)	(96,840)
Accumulated other comprehensive loss	(28)	—
Total Spero Therapeutics, Inc. stockholders' equity	115,500	84,602
Non-controlling interests	355	355
Total stockholders' equity	115,855	84,957
Total liabilities and stockholders' equity	$ 129,006	$ 93,479

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,		
	2018	2017	2016
Grant revenue	$ 3,966	$ 1,979	$ 335
Operating expenses:			
Research and development	33,885	32,869	26,333
General and administrative	12,887	10,840	7,223
Total operating expenses	46,772	43,709	33,556
Loss from operations	(42,806)	(41,730)	(33,221)
Other income (expense):			
Change in fair value of derivative liabilities	—	1,541	580
Interest income and other income (expense), net	1,144	303	—
Total other income (expense), net	1,144	1,844	580
Net loss	(41,662)	(39,886)	(32,641)
Less: Net loss attributable to non-controlling interest	—	(1,143)	(7,150)
Net loss attributable to Spero Therapeutics, Inc.	(41,662)	(38,743)	(25,491)
Cumulative dividends on redeemable convertible preferred shares	—	(6,146)	(3,441)
Accretion of redeemable bridge units and redeemable convertible preferred shares to redemption value	—	(1,208)	(996)
Net loss attributable to common shareholders of Spero Therapeutics, Inc.	$ (41,662)	$ (46,097)	$ (29,928)
Net loss per share attributable to common shareholders per share, basic and diluted	$ (2.60)	$ (17.82)	$ (95.87)
Weighted average shares outstanding, basic and diluted:	16,001,832	2,586,865	312,169
Comprehensive loss:			
Net loss	(41,662)	(39,886)	(32,641)
Other comprehensive loss:	—	—	—
Unrealized loss on marketable securities	(28)	—	—
Total other comprehensive gain loss	(28)	—	—
Total comprehensive loss	$ (41,690)	$ (39,886)	$ (32,641)

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		Series A and B Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Spero Therapeutics, Inc. Stockholders'	Non-controlling	Total Stockholders'
	Units	Amount	Units	Amount	Shares	Amount	Units	Par Value	Shares	Par Value	Shares	Par Value	Capital	Deficit	Equity (Deficit)	Interests	Equity (Deficit)
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
Issuance of common stock upon the exercise of stock options	—	—	—	—	—	—	—	—	—	—	56,780	—	335	—	335	—	335
Issuance of common and Series A preferred stock in public offering, net of issuance costs of $996	—	—	—	—	—	—	—	—	2,220	—	3,780,000	4	69,500	—	69,504	—	69,504
Issuance of Series B preferred stock in exchange for common stock	—	—	—	—	—	—	—	—	1,000	—	(1,000,000)	(1)	1	—	—	—	—
Share-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	2,749	—	2,749	—	2,749
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(28)	—	(28)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	(41,662)	(41,662)	—	(41,662)
Balances at December 31, 2018	—	$ —	—	$ —	—	$ —	—	—	3,220	—	17,205,962	17	254,013	(138,502)	115,500	355	115,855

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

SPERO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	2018	2017	2016
Cash flows from operating activities:			
Net loss	$ (41,662)	$ (39,886)	$ (32,641)
Adjustments to reconcile net loss to net cash used in operating activities:			
Non-cash research and development expense	—	—	4,595
Depreciation and amortization	409	363	279
Loss on disposal of fixed assets	248	—	—
Change in fair value of derivative liabilities	—	(1,541)	(580)
Share-based compensation	2,749	1,427	180
Unrealized foreign currency transaction loss	373	83	—
Accretion of discount on marketable securities	(671)	—	—
Changes in operating assets and liabilities:			
Other receivables	635	(707)	(294)
Prepaid expenses and other current assets	(5,497)	(575)	(966)
Tax incentive receivables	770	(1,811)	(144)
Deposits	—	—	(53)
Accounts payable	84	2,349	(644)
Accrued expenses and other current liabilities	3,575	1,315	2,322
Deferred rent	554	(128)	(84)
Other assets	(1,192)	—	—
Advance payments from collaborator	—	—	(929)
Net cash used in operating activities	(39,625)	(39,111)	(28,959)
Cash flows from investing activities:			
Purchases of marketable securities	(130,175)	—	—
Proceeds from maturities of marketable securities	49,455	—	—
Purchases of property and equipment	(2,436)	(27)	(830)
Net cash used in investing activities	(83,156)	(27)	(830)
Cash flows from financing activities:			
Proceeds from 2018 equity offering	70,500	—	—
Payment of offering costs related to 2018 equity offering	(996)	—	—
Payment of offering costs related to 2018 registration statement and at-the-market-facility	(316)	—	—
Proceeds from stock option exercises	335	—	—
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 bridge units	—	—	8,500
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	69,523	116,111	34,413
Net (decrease) increase in cash and cash equivalents	(53,258)	76,973	4,624
Cash, cash equivalents and restricted cash at beginning of period	87,338	10,365	5,741
Cash, cash equivalents and restricted cash at end of period	34,080	$ 87,338	$ 10,365
Supplemental disclosure of non-cash investing and financing activities:			
Purchases of property and equipment included in accounts payable and accrued expenses	$ 54	$ —	$ —
Conversion of bridge units into preferred units	$ —	$ 8,500	$ —
Conversion of preferred stock to common stock	$ —	$ 107,018	$ —
Settlement of derivative liabilities upon issuance of preferred units	$ —	$ 944	$ —
Issuance of tranche rights with preferred units	$ —	$ —	$ 909
Deemed contribution of capital	$ —	$ —	$ 2,408
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
Accretion of redeemable convertible preferred units and stock to redemption value	$ —	$ 632	$ 969
Accretion of bridge units to redemption value	$ —	$ 576	$ 27
Issuance of additional shares of common stock to minority investors under anti-dilution rights	$ —	$ —	$ 980

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, SPR206 and SPR741, 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 December 3, 2018, the Company filed a universal shelf registration statement on Form S-3 (Registration No. 333-228661) with the SEC, which was declared effective on December 11, 2018, and pursuant to which it registered for sale up to $200.0 million of any combination of its common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that we may determine, including up to $50.0 million of our common stock available for issuance pursuant to an at-the-market offering program sales agreement that it entered into with Cantor Fitzgerald & Co., or Cantor. Under the sales agreement, Cantor may sell the shares by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415 of the Securities Act.

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

In accordance with Accounting Standards Update ("ASU") 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued. Since inception, the Company has funded its operations with proceeds from sales of preferred units (including bridge units, which converted into preferred units), payments received in connection with a concluded collaboration agreement and funding from government contracts, and most recently, with proceeds from the Company's initial public offering ("IPO") completed in November 2017. The Company has incurred recurring losses since inception, including net losses attributable to Spero Therapeutics, Inc. of $41.7 million, $38.7 million and $25.5 million for the years ended December 31, 2018, 2017 and 2016, respectively. In addition, as of December 31, 2018, the Company had an accumulated deficit of $138.5 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, 2018 and 2017, the Company consolidated its non-controlling interest in Spero Gyrase, Inc.

Concentrations of Credit Risk and of Significant Suppliers

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

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

Deferred Offering Costs

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

financing, these costs are recorded in stockholders' deficit as a reduction of additional paid-in capital generated as a result of the offering. Should the planned equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss.

Cash Equivalents

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

Marketable Securities

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

Property and Equipment

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

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

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

Other Assets

Other assets consist of long-term prepayments and deposits.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows. During the year ended December 31, 2018, the Company recorded a loss of $0.2 million related to the write-off of fixed assets at its Watertown, Massachusetts laboratory facility. The Company did not record any impairment losses on long-lived assets during the years ended December 31, 2017 or 2016.

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 Biomedical Advanced Research and Development Authority ("BARDA"), 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 once the Company has substantially accomplished what it must do to be entitled to the benefits represented by the revenues. 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 and through December 31, 2018, 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 personnel salaries, share-based compensation and benefits, allocated facilities costs, depreciation, manufacturing expenses, costs related to the Company's government contract and grant arrangements, and external costs of outside vendors engaged to conduct preclinical development activities, clinical trials as well as the cost of licensing technology. Upfront payments and milestone payments made for the licensing of technology are expensed as research and development in the period in which they are incurred. Advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed.

Clinical Trial and other Research Contract Costs and Accruals

The Company has entered into various research and development contracts with clinical research organizations and other companies both inside and outside of the United States. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. There may be instances in which payments made to these vendors exceed the level of service provided and will result in a prepayment of the expense. The Company records accruals for estimated ongoing research and clinical trial costs based on the services received and efforts expended pursuant to multiple contracts with these vendors. When evaluating the adequacy of the accrued liabilities, the Company analyzes the progress of the studies or trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

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

Share-Based Compensation

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

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with shareholders. For the year ended December 31, 2018, these changes related to unrealized gains and losses on the Company's available-for-sale marketable securities. There were no reclassifications out of comprehensive loss for the year ended December 31, 2018. There was no difference between net loss and comprehensive loss for the years ended December 31, 2017 and 2016.

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, 2018, 2017 and 2016.

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 May 2014, the Financial Accounting Standards Board ("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 Licensin*g, 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 adopted this standard using the modified retrospective approach, however the Company determined that government grant revenue is outside the scope of ASC 606. Therefore, the adoption of ASC 606 did not impact the Company's financial position, results of operations or cash flows as its only existing revenue source as of December 31, 2018 is government grants.

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's adoption of ASU 2016-15 did not have a material impact on the Company's 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. The adoption of ASU 2016-18 did not have a material impact on the Company's consolidated financial statements. The inclusion of restricted cash increased the beginning and ending balances of the consolidated statement of cash flows by $50,000 for the years ended December 31, 2017 and 2016.

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 adoption of ASU 2017-01 did not materially impact the Company's 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 adoption of ASU 2017-09 did not materially impact the Company's consolidated financial statements.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"), which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e., lessees and lessors), and will replace the existing guidance in ASC840, *Leases*. The FASB subsequently issued amendments to ASU 2016-02, which have the same effective date and transition date of January 1, 2019: (i) ASU No. 2018-10, *Codification Improvements to Topic 842, Leases*, which amends certain narrow aspects of the guidance issued in ASU 2016-02; and (ii) ASU 2018-11, *Leases (Topic 842): Targeted Improvements*, which allows for a transition approach to initially apply ASU 2016-02 at the adoption date and recognize a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption as well as an additional practical expedient for lessors to not separate non-lease components from the associated lease component. ASU 2016-02 requires lessees to classify leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use, or ROU, asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases 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 has elected to adopt ASU 2016-02 effective January 1, 2019 through a cumulative-effect adjustment under ASU 2018-11. This standard provides a number of optional practical expedients in transition. The Company plans to apply the package of practical expedients to leases that commenced prior to the effective date whereby it will elect to not reassess the following: (i) whether any expired or existing contracts contain leases; (ii) the lease classification for any expired or existing leases; and (iii) initial direct costs for any existing leases. The Company expects to elect the short-term lease recognition exemption for all leases that qualify, where a right-of-use asset or lease liability will not be recognized for short term leases. The Company has substantially completed its assessment of the adoption of ASU 2016-02 and expects that the most significant effects of adoption will be to the recognition of material new ROU assets and corresponding liabilities on its consolidated balance sheet related to its existing facility operating leases (see Note 11).

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 does not expect the adoption of this standard will have a material impact to its consolidated statement of operations.

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

3. Fair Value of Financial Assets and Liabilities

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

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

	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

The tables above do not include cash of $5.4 million and $4.2 million as of December 31, 2018 and 2017, respectively. During the years ended December 31, 2018 and 2017, there were no transfers between Level 1, Level 2 and Level 3.

Marketable Securities

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

The following table summarizes the gross unrealized gains and losses of the Company's marketable securities as of December 31, 2018 (in thousands):

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets:				
U.S. government securities	$ 37,819	$ —	$ (4)	$ 37,815
Corporate bonds	26,696	—	(24)	26,672
Commercial paper	16,876	—	—	16,876
	$ 81,391	$ —	$ (28)	$ 81,363

As of December 31, 2018, all of the Company's marketable securities had remaining contractual maturity dates of one year or less from the consolidated balance sheet date. The Company did not own any marketable securities as of December 31, 2017.

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, 2018 and 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.

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
Change in fair value	—	—	—	—
Balance at December 31, 2018	$ —	$ —	$ 223	$ 223

4. Property and Equipment, Net

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

	December 31,	
	2018	2017
Computer software and equipment	$ 166	$ 181
Office furniture and equipment	210	201
Leasehold improvements	863	915
Laboratory equipment	—	510
Construction-in-progress	897	—
Manufacturing equipment	1,584	—
	3,720	1,807
Less: Accumulated depreciation and amortization	(827)	(643)
	$ 2,893	$ 1,164

Property and equipment additions during the year ended December 31, 2018, primarily related to leased manufacturing equipment which was fully paid by the Company, as well as construction-in-progress and leasehold improvements related to the expansion of Company's leased office space (see Note 11). Depreciation and amortization expense was $0.4 million, $0.4 million and less than $0.3 million for the years ended December 31, 2018, 2017 and 2016, respectively. During the year ended December 31, 2018, the Company recorded a loss of $0.2 million related to the write off of laboratory equipment and certain leasehold improvements at its Watertown, Massachusetts laboratory facility.

5. Accrued Expenses and Other Current Liabilities

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

	December 31,	
	2018	2017
Accrued external research and development expenses	$ 4,541	$ 1,770
Accrued payroll and related expenses	2,379	1,369
Accrued professional fees	917	878
Accrued other	426	304
	$ 8,263	$ 4,321

6. Convertible Preferred Shares

Series A Convertible Preferred Shares

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

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

Series B Convertible Preferred Shares

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

Each share of Series B Preferred Stock is convertible into 1,000 shares of Common Stock at any time at the option of the holder, provided that the holder will be prohibited from converting the Series B Preferred Stock into shares of Common Stock if, as a result of such conversion, the holder, together with its affiliates, would own more than 9.99% of the total number of shares of Common Stock then issued and outstanding, subject to certain exceptions. In the event of the Company's liquidation, dissolution, or winding up, holders of Series B Preferred Stock will receive a payment equal to $0.001 per share of Series B Preferred Stock before any proceeds are distributed to the holders of Common Stock and equal to any distributions to the holders of the Series A Convertible Preferred

Stock. The Series B Convertible Preferred Stock does not have any mandatory redemption rights or other redemption rights that would be outside of the Company's control. As such, the Company has classified the Series B Convertible Preferred Stock within permanent equity in its consolidated balance sheet.

Redeemable Convertible Preferred Shares

Prior to the Reorganization (see Note 1), 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 Company's Reorganization on June 30, 2017, 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, and 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 were the same both before and after the Reorganization. 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, all of the then outstanding convertible preferred shares automatically converted into shares of common stock.

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. The option was settled in June 2015 upon the issuance of Class A preferred units, as discussed below.

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.

The Junior preferred stock, the Series A preferred stock, the Series B preferred stock and the Series C preferred stock that were outstanding prior to the Company's IPO in November 2017 are collectively referred to as the "Preferred Stock".

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. On June 30, 2017, pursuant to the terms of the Reorganization (see Note 1), the then 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.

On November 6, 2017, Spero Therapeutics, Inc. completed an 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).

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

On December 3, 2018, the Company filed a universal shelf registration statement on Form S-3 (Registration No. 333-228661) with the SEC, which was declared effective on December 11, 2018, and pursuant to which the Company registered for sale up to $200.0 million of any combination of its common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that it may determine, including up to $50.0 million of its common stock available for issuance pursuant to an at-the-market offering program sales agreement that it entered into with Cantor Fitzgerald & Co. Under the sales agreement, Cantor may sell shares of the Company's common stock by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415 of the Securities Act, subject to the terms of the sales agreement. As of December 31, 2018, there have been no sales of the Company's common stock under the sales agreement. The Company incurred approximately $0.3 million of costs related to the shelf registration statement and at the market offering. These costs have been classified as deferred offering costs on the Company's balance sheet as of December 31, 2018, and will be charged to additional paid-in-capital on a prorated basis upon the issuance of the associated equity.

8. Share-Based Compensation

Incentive Stock Units

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

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

2017 Stock Incentive Plan

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

cancelled, repurchased or are otherwise terminated by the Company under the 2017 Plan will be added back to the shares of common stock available for issuance under the 2017 Plan.

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

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

On October 18, 2017, the Company's stockholders approved an amendment to the 2017 Plan, which became effective upon the completion of the Company's IPO, to increase the total number of shares reserved for issuance under the 2017 Plan from 1,785,416 to 2,696,401. Additionally, the number of shares of common stock that may be issued under the 2017 Plan will automatically increase on each January 1, beginning with the fiscal year ending December 31, 2019 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2027, equal to the lowest of (i) 607,324 shares of common stock, (ii) 4% of the outstanding shares of common stock on such date and (iii) an amount determined by the Company's board of directors or compensation committee. As of December 31, 2018, there were 341,811 shares remaining available to be issued under the 2017 Plan.

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,		
	2018	2017	2016
Risk-free interest rate	2.7%	2.0%	1.3%
Expected term (in years)	6.3	6.1	6.3
Expected volatility	74.1%	77.1%	76.5%
Expected dividend yield	0.0%	0.0%	0.0%

The following table summarizes stock option activity during 2018:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2017	2,011,296	$ 7.24	9.38	$ 9,074
Granted	503,730	11.30		
Exercised	(56,780)	5.90		
Forfeited	(160,436)	9.13		
Cancelled	—	—		
Outstanding as of December 31, 2018	2,297,810	$ 8.03	8.77	$ 354
Outstanding as of December 31, 2018 - vested and expected to vest	2,294,629	$ 8.03	8.62	$ 354
Exercisable at December 31, 2018	845,851	$ 6.69	8.57	$ 183

The weighted average grant-date fair value of stock options granted during the year ended December 31, 2018 was $7.63 per share. The weighted average grant-date fair value of awards granted during the years ended December 31, 2017 and 2016 was $4.72 per share and $3.40 per unit, respectively. The aggregate intrinsic value of stock options exercised during the year ended December 31, 2018 was approximately $0.3 million. There were no stock options exercised during the years ended December 31, 2017 and 2016. The Company satisfies stock option exercises with newly issued shares of its common stock.

As of December 31, 2018, total unrecognized compensation cost related to unvested stock option grants was approximately $7.9 million. This amount is expected to be recognized over a weighted average period of approximately 2.7 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,		
	2018	2017	2016
Research and development expenses	$ 1,072	$ 371	$ 66
General and administrative expenses	1,677	1,056	114
Total	$ 2,749	$ 1,427	$ 180

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 then CAI-held NIAID contract to the Company, which was finalized in December 2017. The NIAID contract provides for development funding of up to $6.3 million over a base and three option periods. To date, funding for the base period and the first two option periods totaling $5.7 million have been committed. The Company shall pay PBB a percentage of funds received from NIAID up to a maximum of $1.3 million, of which $0.3 million was paid upfront to PBB as part of this agreement, as described below. During the year ended December 31, 2018, the Company recorded $0.4 million of expense related to amounts payable to PBB under this agreement.

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 December 31, 2018 and 2017, the Company's only remaining non-controlling interest relates to Spero Gyrase, Inc., which totaled $0.4 million.

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, 2018, 2017 and 2016, 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,		
	2018	2017	2016
Domestic	$ (33,236)	$ (38,706)	$ (27,148)
Foreign	(8,426)	(1,180)	(5,493)
Loss before income taxes	$ (41,662)	$ (39,886)	$ (32,641)

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,		
	2018	2017	2016
Federal statutory income tax rate	(21.0)	(34.0)	(34.0)
Federal and state research and development tax credit	(2.6)	(3.3)	(1.7)
State taxes, net of federal benefit	(5.4)	(5.3)	(4.4)
Foreign rate differential	1.9	0.1	2.3
Nondeductible items	1.2	(0.1)	4.8
Effect of US tax reform	—	23.8	—
Increase in deferred tax asset valuation allowance	25.9	18.8	33.0
Effective income tax rate	—	—	—

Net deferred tax assets as of December 31, 2018 and 2017 consisted of the following (in thousands):

	December 31,	
	2018	2017
Net operating loss carryforwards	$ 29,025	$ 21,754
Research and development tax credit carryforwards	3,385	2,022
Other	1,731	743
Total deferred tax assets	34,141	24,519
Valuation allowance	(34,141)	(24,519)
Net deferred tax assets	$ —	$ —

As of December 31, 2018, the Company had U.S. federal and state net operating loss carryforwards of $100.4 million and $100.3 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2033. In addition, as of December 31, 2018, the Company had foreign net operating loss carryforwards of $11.7 million, which may be available to offset future income tax liabilities and do not expire. As of December 31, 2018, the Company also had federal and state research and development tax credit carryforwards of $2.6 million and $0.8 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, 2018 and 2017. 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, 2018 and 2017 related primarily to the increase in net operating loss carryforwards and research and development tax credit carryforwards, and were as follows (in thousands):

	December 31,	
	2018	2017
Valuation allowance as of beginning of year	$ (24,519)	$ (17,152)
Decreases recorded as benefit to income tax provision	—	—
Increases recorded to income tax provision	(9,622)	(7,367)
Valuation allowance as of end of year	$ (34,141)	$ (24,519)

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2018 or 2017. 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, 2018 or 2017, 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 2015. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state authorities to the extent utilized in a future period. No federal or state tax audits are currently in process.

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

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

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 occurred on December 22, 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. The Amendment also includes a provision from the landlord of $0.4 million for leasehold improvements on the Expansion Premises.

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, 2018 (in thousands):

Year Ending December 31,		
2019	$	1,361
2020		1,054
2021		995
2022		1,107
2023		1,123
2024		1,138
2025		1,108
	$	7,886

Rent expense for the years ended December 31, 2018, 2017 and 2016 was $0.8 million, $0.8 million and $0.4 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, 2018, 2017 or 2016.

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

BARDA

In July 2018, the Company was awarded a contract from BARDA of up to $44.2 million to develop SPR994 for the treatment of complicated urinary tract infections ("cUTIs") caused by antibiotic resistant Gram-negative bacteria and for assessment against biodefense pathogens. The award commits initial funding of $15.7 million over a three-year base period from July 1, 2018 to June 30, 2021 for cUTI development activities. The balance of the award is subject to BARDA exercising two options. The exercise of the first option would entail funding of $13.6 million and is exercisable by BARDA subject to the Company achieving specified milestones related to, among other things, clinical progress and data. The exercise of the second option would entail funding of $14.9 million and is exercisable by BARDA subject to, among other things, satisfactory progress and results from the biodefense studies described below.

As part of an inter-agency collaboration between BARDA and the Defense Threat Reduction Agency ("DTRA"), a series of studies to assess the efficacy of SPR994 in the treatment of infections caused by biodefense threats such as anthrax, plague and melioidosis will be conducted by the U.S. Army Medical Research Institute of Infectious Diseases ("USAMRIID") under the direction of Spero. Because the FDA requires data from a human pneumonic disease as supportive of use of an antibiotic to treat a biothreat infection, the scope of the BARDA award includes the assessment of SPR994 levels in the lung of healthy volunteers as well as a proof of concept clinical trial in pneumonia patients, an indication for which tebipenem, SPR994's active pharmaceutical ingredient, is currently approved in Japan for pediatric use. The Company recorded $1.4 million of revenue under this agreement, of which $0.3 million was invoiced but unpaid and included in other receivables at December 31, 2018.

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, 2018, the Company recognized $0.3 million of revenue under this agreement, of which less than $0.1 million was invoiced but unpaid and included in other receivables at December 31, 2018.

NIAID

In February 2017, the Company was awarded a grant from NIAID to conduct additional preclinical studies of SPR720, the Company's novel oral bacterial gyrase inhibitor, for the treatment of non-tuberculous mycobacterial infections. The award is structured as a 12-month $0.6 million base period and $0.4 million option period. In February 2018 NIAID exercised the $0.4 million 12-month option period. In January 2019, the period of performance for this award was extended for an additional 12-month period. The Company recognized $0.5 million of revenue in the year ended December 31, 2018 under this agreement, of which less than $0.1 million was invoiced but unpaid and included in other receivables at December 31, 2018.

In June 2016, the Company entered into agreements with Pro Bono Bio PLC ("PBB"), a corporation organized under the laws of England, and certain of its affiliates, including PBB Distributions Limited and Cantab Anti-Infectives Limited ("CAI"), in order to acquire certain intellectual property and government funding arrangements relating to SPR206. Under these agreements, CAI agreed to submit a request to NIAID to assign the then CAI-held NIAID contract to Spero, which was finalized in December 2017. The NIAID contract provides for development funding of up to $6.3 million over a base period and three option periods. As of December 31, 2018, funding for the base period and the first two option periods totaling $5.7 million have been committed. Spero shall pay PBB a percentage of funds received from NIAID up to a maximum of $1.3 million, of which $0.3 million was paid upfront to PBB as part

of the agreement. The Company recorded $1.3 million of revenue under this agreement during the year ended December 31, 2018, of which less than $0.1 million was invoiced but unpaid and included in other receivables at December 31, 2018. During the year ended December 31, 2018, the Company recorded approximately $0.4 million in expense associated with amounts payable to PBB under this agreement, which has been included within research and development expenses within the consolidated statement of operations and comprehensive loss.

CARB-X

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

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 for the year ended December 31, 2016.

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 ($6.4 million and $6.7 million as of December 31, 2018 and 2017, respectively)) upon the achievement of a specified commercial milestone. In addition, the Company has agreed to pay to PBB royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement. During the year ended December 31, 2018, the Company recorded $0.2 million in research and development expense related to the achievement of regulatory milestones for SPR206.

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

Vertex License Agreement

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

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

Meiji License Agreement

In June 2017, the Company entered into agreements with Meiji Seika Pharma Co. Ltd. ("Meiji"), a Japanese corporation, whereby Meiji granted to the Company certain know-how and a license to research, develop, manufacture and sell products for a proprietary compound in the licensed territory. In exchange for the know-how and license, the Company paid Meiji an upfront, one-time, nonrefundable, non-creditable fee of $0.6 million, which was recognized as research and development expense. As part of the agreement, the Company is obligated to make milestone payments of up to $3.0 million upon the achievement of specified clinical and regulatory milestones, to pay royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement and to pay Meiji a low double-digit percentage of any sublicense fees received by the Company up to $7.5 million. In October 2017, the Company paid a $1.0 million milestone payment to Meiji upon the enrollment of the first patient in the Company's Phase 1 clinical trial of 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. During the three

months ended December 31, 2018, the Company paid Meiji $1.6 million related to fixed assets which will be used in manufacturing related activities at Meiji. This equipment has been capitalized as property and equipment in the consolidated balance sheet as of December 31, 2018.

The agreement continues in effect until the expiration of all payment obligations thereunder (including royalty payments and licensee revenue) on a product-by-product and country-by-country basis, unless earlier terminated by the parties. Pursuant to the terms of the agreement, in addition to each party's right to terminate the agreement upon the other party's material breach (if not cured within a specified period after receipt of notice) or insolvency, the Company also has unilateral termination rights (i) in the event that the Company abandons the development and commercialization of 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, 2018, 2017 and 2016, $1.2 million, $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, 2018 and 2017, the Company's tax incentive receivables from the Australian government totaled $1.1 million and $1.9 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,		
	2018	2017	2016
Numerator:			
Net loss	$ (41,662)	$ (39,886)	$ (32,641)
Less: Net loss attributable to non-controlling interests	—	(1,143)	(7,150)
Plus: Cumulative dividends on redeemable convertible preferred shares	—	(6,146)	(3,441)
Plus: Accretion of bridge units and redeemable convertible preferred shares to redemption value	—	(1,208)	(996)
Net loss attributable to common stockholders of Spero Therapeutics, Inc.	$ (41,662)	$ (46,097)	$ (29,928)
Denominator:			
Weighted average common shares outstanding, basic and diluted	16,001,832	2,586,865	312,169
Net loss per share attributable to common stockholders of Spero Therapeutics, Inc., basic and diluted	$ (2.60)	$ (17.82)	$ (95.87)

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,		
	2018	2017	2016
Options to purchase common stock	2,297,810	2,011,296	—
Series A convertible preferred stock (as converted to common shares)	2,220,000	—	—
Series B convertible preferred stock (as converted to common shares)	1,000,000	—	—
Redeemable convertible preferred shares (as converted to common shares)	—	—	2,229,518
Incentive units	—	—	413,266
	5,517,810	2,011,296	2,642,784

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, 2018, 2017 and 2016.

17. Quarterly Financial Data (unaudited)

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

	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	(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

18. Subsequent Events

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

Under the terms of the License Agreement, the Company received an upfront payment of $3.0 million. The Company may also receive up to an additional $59.5 million in milestone payments upon Everest's achievement of certain developmental, regulatory and sales milestone events related to SPR206, which achievement cannot be guaranteed. The Company is also entitled to receive high single-digit to low double-digit royalties on net sales, if any, of Licensed Products in the Territory following regulatory approval of the Compound. Everest has the right to sublicense to affiliates and third parties in the Territory. Everest is responsible for all costs related to developing, obtaining regulatory approval of and commercializing the Compound and Licensed Products in the Territory, and is obligated to use commercially reasonable efforts to develop, manufacture and commercialize Licensed Products, including to achieve certain specified diligence milestones within agreed-upon periods. Unless earlier terminated due to certain material breaches of the contract, or otherwise, the License Agreement will expire on a jurisdiction-by-jurisdiction and Licensed Product-by-Licensed Product basis until the latest to occur of expiration of the last valid claim under a licensed patent in such jurisdiction, the expiration of regulatory exclusivity in such jurisdiction or ten years after the first commercial sale of such Licensed Product in such jurisdiction. The License Agreement may be terminated in its entirety by Everest upon 90 or 180 days' prior written notice, depending on the stage of development of the initial Licensed Product.

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, 2018. 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, 2018, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Controls Over Financial Reporting

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

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the 2013 framework in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under that framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2018.

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

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended December 31, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Adoption of Inducement Equity Incentive Plan

On March 11, 2019, we adopted the 2019 Inducement Equity Incentive Plan (the "Plan") to reserve 331,500 shares of our common stock to be used exclusively for grants of awards to individuals that were not previously employees or directors of Spero, as a material inducement to the individual's entry into employment with us within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. The Plan was approved by our Board of Directors without stockholder approval pursuant to Rule 5635(c)(4), and the terms and conditions of the Plan are substantially similar to our stockholder-approved 2017 Stock Incentive Plan, as amended. A complete copy of the Plan and the Form of Stock Option Grant Notice and Stock Option Agreement under the Plan are filed herewith as Exhibits 10.3 and 10.4, respectively, and are incorporated herein by reference. The above summary of the terms of the Plan and Plan documents does not purport to be complete and is qualified in its entirety by reference to such exhibits.

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 2019 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" and "Management and Corporate Governance Matters -- Compensation Committee Interlocks and Insider Participation" in our proxy statement for the 2019 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 Plans and Other Benefits Plans" in our proxy statement for the 2019 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 our proxy statement for the 2019 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 our proxy statement for the 2019 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 3.2)	11/6/2017	001-38266
3.3	Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	7/17/2018	001-38266
3.4	Certificate of Designation of Preferences, Rights and Limitations of Series B Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	11/16/2018	001-38266
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	001-38266
10.2#	Form of Stock Option Agreement under the 2017 Stock Incentive Plan, as amended		Form 10-Q (Exhibit 10.2)	12/14/2017	001-38266
10.3#	2019 Inducement Equity Incentive Plan	X			
10.4#	Form of Stock Option Agreement under the 2019 Inducement Equity Incentive Plan	X			
10.5#	Form of Director and Officer Indemnification Agreement		Form S-1 (Exhibit 10.4)	10/6/2017	333-220858
10.6#	Non-Employee Director Compensation Policy		Form S-1/A (Exhibit 10.20)	10/23/2017	333-220858
10.7#	Employment Agreement, dated October 20, 2017, by and between the Registrant and Ankit Mahadevia, M.D.		Form S-1/A (Exhibit 10.5)	10/23/2017	333-220858
10.8#	Employment Agreement, dated October 20, 2017, by and between the Registrant and Joel Sendek		Form S-1/A (Exhibit 10.6)	10/23/2017	333-220858
10.9#	Employment Agreement, dated October 20, 2017, by and between the Registrant and Thomas Parr Jr., Ph.D.		Form S-1/A (Exhibit 10.7)	10/23/2017	333-220858

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
10.10#	Employment Agreement, dated October 20, 2017, by and between the Registrant and Cristina Larkin		Form S-1/A (Exhibit 10.8)	10/23/2017	333-220858
10.11#	Employment Agreement, dated December 13, 2017, by and between the Registrant and David Melnick, M.D.		Form 10-K (Exhibit 10.9)	4/2/2018	001-38266
10.12#	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†	Contract Award, dated July 12, 2018, issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services		Form 10-Q (Exhibit 10.1)	11/8/2018	001-38266
10.20*	License Agreement, dated January 4, 2019, by and between New Pharma License Holdings Limited and Everest Medicines II Limited	X			
10.21	Exchange Agreement, dated November 15, 2018, by and among Spero Therapeutics, Inc. and Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., Biotechnology Value Trading Fund OS, L.P. and MSI BVF SPV LLC		Form 8-K (Exhibit 10.1)	11/16/2018	001-38266
10.22	Controlled Equity Offering Sales Agreement, dated December 3, 2018, by and between the Registrant and Cantor Fitzgerald & Co.		Form S-3 (Exhibit 1.2)	12/3/2018	333-228661
10.23	Form of Proprietary Information and Inventions Assignment Agreement		Form S-1/A (Exhibit 10.17)	10/23/2017	333-220858

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
16.1	Letter of KPMG LLP, dated August 25, 2017, regarding changes in the Registrant's certifying accountants		Form S-1 (Exhibit 16.1)	10/6/2017	333-220858
21.1	List of Subsidiaries of the Registrant	X			
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm	X			
31.1	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X			
31.2	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X			
32.1	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X			
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X			
101.INS	XBRL Instance Document	X			
101.SCH	XBRL Taxonomy Extension Schema Document	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	XBRL Taxonomy Extension Definition	X			
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	XBRL Taxonomy Presentation Linkbase Document	X			

† Confidential treatment received as to portions of the exhibit. Confidential materials omitted and filed separately with the SEC.
# Management contract or compensatory plan.
* Confidential treatment requested for portions of this exhibit. Confidential materials omitted and filed separately with the SEC.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, 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: March 14, 2019

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)*	March 14, 2019
/s/ Joel Sendek Joel Sendek	Chief Financial Officer and Treasurer *(Principal Financial Officer and Principal Accounting Officer)*	March 14, 2019
/s/ Milind Deshpande, Ph.D. Milind Deshpande, Ph.D.	Director	March 14, 2019
/s/ Jean-François Formela, M.D. Jean-François Formela, M.D.	Director	March 14, 2019
/s/ John C. Pottage, M.D. John C. Pottage, M.D.	Director	March 14, 2019
/s/ David P. Southwell David P. Southwell	Director	March 14, 2019
/s/ Frank E. Thomas Frank E. Thomas	Director	March 14, 2019
/s/ Patrick Vink, M.D. Patrick Vink, M.D.	Director	March 14, 2019

Exhibit 10.3

SPERO THERAPEUTICS, INC.

2019 Inducement Equity Incentive Plan

(Adopted March 11, 2019)

1. DEFINITIONS.

Unless otherwise specified or unless the context otherwise requires, the following terms, as used in this Spero Therapeutics, Inc. 2019 Inducement Equity Incentive Plan, have the following meanings:

Administrator means the Board of Directors, unless it has delegated power to act on its behalf to the Committee, in which case the term Administrator means the Committee.

Affiliate means a corporation or other entity which, for purposes of Section 424 of the Code, is a parent or subsidiary of the Company, direct or indirect.

Agreement means an agreement between the Company and a Participant delivered pursuant to the Plan and pertaining to a Stock Right, in such form as the Administrator shall approve.

Board of Directors means the Board of Directors of the Company.

Cause means, with respect to a Participant (a) dishonesty with respect to the Company or any Affiliate, (b) insubordination, substantial malfeasance or non-feasance of duty, (c) unauthorized disclosure of confidential information, (d) breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or similar agreement between the Participant and the Company or any Affiliate, and (e) conduct substantially prejudicial to the business of the Company or any Affiliate; provided, however, that any provision in an agreement between the Participant and the Company or an Affiliate, which contains a conflicting definition of Cause for termination and which is in effect at the time of such termination, shall supersede this definition with respect to that Participant. The determination of the Administrator as to the existence of Cause will be conclusive on the Participant and the Company.

Code means the United States Internal Revenue Code of 1986, as amended including any successor statute, regulation and guidance thereto.

Committee means the Company's compensation committee (as constituted in compliance with Rule 5605(d)(2) of the Nasdaq Listing Rules) in order to comply with the exemption from the stockholder approval requirement for "inducement grants" provided under Rule 5635(c)(4) of the Nasdaq Listing Rules.

Common Stock means shares of the Company's common stock, $0.001par value per share.

Company means Spero Therapeutics, Inc., a Delaware corporation.

Consultant means any natural person who is an advisor or consultant who provides bona fide services to the Company or its Affiliates, provided that such services are not in connection with the offer or sale of securities in a capital raising transaction, and do not directly or indirectly promote or maintain a market for the Company's or its Affiliates' securities.

Disability or Disabled means permanent and total disability as defined in Section 22(e)(3) of the Code.

Employee means any employee of the Company or of an Affiliate, designated by the Administrator to be eligible to be granted one or more Stock Rights under the Plan.

Exchange Act means the United States Securities Exchange Act of 1934, as amended.

Fair Market Value of a Share of Common Stock means:

(1) If the Common Stock is listed on a national securities exchange or traded in the over-the-counter market and sales prices are regularly reported for the Common Stock, the closing or, if not applicable, the last price of the Common Stock on the composite tape or other comparable reporting system for the trading day on the applicable date and if such applicable date is not a trading day, the last market trading day prior to such date;

(2) If the Common Stock is not traded on a national securities exchange but is traded on the over-the-counter market, if sales prices are not regularly reported for the Common Stock for the trading day referred to in clause (1), and if bid and asked prices for the Common Stock are regularly reported, the mean between the bid and the asked price for the Common Stock at the close of trading in the over-the-counter market for the most recent trading day on which Common Stock was traded on the applicable date and if such applicable date is not a trading day, the last market trading day prior to such date; and

(3) If the Common Stock is neither listed on a national securities exchange nor traded in the over-the-counter market, such value as the Administrator, in good faith, shall determine in compliance with applicable laws.

ISO means an option intended to qualify as an incentive stock option under Section 422 of the Code.

Non-Qualified Option means an option which is not intended to qualify as an ISO.

Option means a Non-Qualified Option granted under the Plan.

Participant means an Employee of the Company or an Affiliate to whom one or more Stock Rights are granted under the Plan. As used herein, "Participant" shall include "Participant's Survivors" where the context requires.

Plan means the Spero Therapeutics, Inc. 2019 Inducement Equity Incentive Plan.

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

Shares means shares of the Common Stock as to which Stock Rights have been or may be granted under the Plan or any shares of capital stock into which the Shares are changed or for which they are exchanged within the provisions of Paragraph 3 of the Plan. The Shares issued under the Plan may be authorized and unissued shares or shares held by the Company in its treasury, or both.

Stock-Based Award means a grant by the Company under the Plan of an equity award or an equity based award which is not an Option or a Stock Grant.

Stock Grant means a grant by the Company of Shares under the Plan.

Stock Right means a right to Shares or the value of Shares of the Company granted pursuant to the Plan – a Non-Qualified Option, a Stock Grant or a Stock-Based Award.

Survivor means a deceased Participant's legal representatives and/or any person or persons who acquired the Participant's rights to a Stock Right by will or by the laws of descent and distribution.

2. PURPOSES OF THE PLAN.

The Plan is intended to advance the interests of the Company's stockholders by enhancing the Company's ability to attract new Employees who are expected to make important contributions to the Company and by providing such persons with equity ownership opportunities that are intended to better align the interests of such persons with those of the Company's stockholders. The Company intends that the Plan be reserved for persons to whom the Company may issue securities without stockholder approval as an inducement pursuant to Listing Rule 5635(c)(4) of the corporate governance rules of the Nasdaq Stock Market.

3. SHARES SUBJECT TO THE PLAN.

(a) The number of Shares which may be issued from time to time pursuant to this Plan shall be 331,500 of shares of Common Stock, or the equivalent of such number of Shares after the Administrator, in its sole discretion, has interpreted the effect of any stock split, stock dividend, combination, recapitalization or similar transaction in accordance with Paragraph 24 of the Plan.

(b) If an Option ceases to be "outstanding", in whole or in part (other than by exercise), or if the Company shall reacquire at not more than its original issuance price any Shares issued pursuant to a Stock Grant or Stock-Based Award, or if any Stock Right expires or is forfeited, cancelled, or otherwise terminated or results in any Shares not being issued, the unissued or reacquired Shares which were subject to such Stock Right shall again be available for issuance from time to time pursuant to this Plan. Notwithstanding the foregoing, if a Stock Right is exercised, in whole or in part, by tender of Shares or if the Company or an Affiliate's tax withholding obligation is satisfied by withholding Shares, the number of Shares deemed to have been issued under the Plan for purposes of the limitation set forth in Paragraph 3(a) above shall

be the number of Shares that were subject to the Stock Right or portion thereof, and not the net number of Shares actually issued.

4. ADMINISTRATION OF THE PLAN.

The Administrator of the Plan will be the Board of Directors, except to the extent the Board of Directors delegates its authority to the Committee, in which case the Committee shall be the Administrator. Subject to the provisions of the Plan, the Administrator is authorized to:

(a) Interpret the provisions of the Plan and all Stock Rights and to make all rules and determinations which it deems necessary or advisable for the administration of the Plan;

(b) Determine which Employees shall be granted Stock Rights;

(c) Determine the number of Shares for which a Stock Right or Stock Rights shall be granted and specify the terms and conditions upon which Stock Rights may be granted;

(d) Amend any term or condition of any outstanding Stock Right, including, without limitation, to reduce or increase the exercise price or purchase price, accelerate the vesting schedule or extend the expiration date, provided that (i) such term or condition as amended is permitted by the Plan; (ii) any such amendment shall not impair the rights of a Participant under any Stock Right previously granted without such Participant's consent or in the event of death of the Participant the Participant's Survivors; and (iii) any such amendment shall be made only after the Administrator determines whether such amendment would cause any adverse tax consequences to the Participant;

(e) Buy out for a payment in cash or Shares, a Stock Right previously granted and/or cancel any such Stock Right and grant in substitution therefor other Stock Rights, covering the same or a different number of Shares and having an exercise price or purchase price per share which may be lower or higher than the exercise price or purchase price of the cancelled Stock Right, based on such terms and conditions as the Administrator shall establish and the Participant shall accept; and

(f) Adopt any sub-plans applicable to residents of any specified jurisdiction as it deems necessary or appropriate in order to comply with or take advantage of any tax or other laws applicable to the Company, any Affiliate or to Participants or to otherwise facilitate the administration of the Plan, which sub-plans may include additional restrictions or conditions applicable to Stock Rights or Shares issuable pursuant to a Stock Right;

provided, however, that all such interpretations, rules, determinations, terms and conditions shall be made and prescribed in the context of not causing any adverse tax consequences under Section 409A of the Code. Subject to the foregoing, the interpretation and construction by the Administrator of any provisions of the Plan or of any Stock Right granted under it shall be final, unless otherwise determined by the Board of Directors, if the Administrator is the Committee. In addition, if the Administrator is the Committee, the Board of Directors may take any action under the Plan that would otherwise be the responsibility of the Committee.

Notwithstanding the foregoing, any grants of Stock Rights under the Plan made by the Board of Directors must be approved by the majority of the Company's independent directors (as defined in Rule 5605(a)(2) of the Nasdaq Listing Rules) in order to comply with Nasdaq Listing Rule 5635(c)(4).

5. ELIGIBILITY FOR PARTICIPATION.

The Administrator will, in its sole discretion, name the Participants in the Plan; provided, however, that each Participant must be an Employee of the Company or of an Affiliate at the time a Stock Right is granted. Notwithstanding the foregoing, the Administrator may authorize the grant of a Stock Right to a person not then an Employee of the Company or of an Affiliate; provided, however, that the actual grant of such Stock Right shall be conditioned upon such person becoming eligible to become a Participant at or prior to the time of the execution of the Agreement evidencing such Stock Right. Non-Qualified Options, Stock Grants and Stock-Based Awards may be granted to any Employee of the Company or an Affiliate. The granting of any Stock Right to any individual shall neither entitle that individual to, nor disqualify him or her from, participation in any other grant of Stock Rights or any grant under any other benefit plan established by the Company or any Affiliate for Employees.

6. TERMS AND CONDITIONS OF OPTIONS.

Each Option shall be set forth in writing in an Option Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Administrator may provide that Options be granted subject to such terms and conditions, consistent with the terms and conditions specifically required under this Plan, as the Administrator may deem appropriate. The Option Agreements shall be subject to at least the following terms and conditions:

(a) Non-Qualified Options: Each Option shall be a Non-Qualified Option and shall be subject to the terms and conditions which the Administrator determines to be appropriate and in the best interest of the Company, subject to the following minimum standards for any such Non-Qualified Option:

(i) Exercise Price: Each Option Agreement shall state the exercise price (per share) of the Shares covered by each Option, which exercise price shall be determined by the Administrator and shall be at least equal to the Fair Market Value per share of the Common Stock on the date of grant of the Option.

(ii) Number of Shares: Each Option Agreement shall state the number of Shares to which it pertains.

(iii) Vesting Periods: Each Option Agreement shall state the date or dates on which it first is exercisable and the date after which it may no longer be exercised, and may provide that the Option rights accrue or become exercisable in installments over a period of months or years, or upon the occurrence of certain conditions or the attainment of stated performance goals or events.

(iv) Additional Conditions: Exercise of any Option may be conditioned upon the Participant's execution of a Share purchase agreement in a form satisfactory to the Administrator providing for certain protections for the Company and its other shareholders, including requirements that:

A. The Participant's or the Participant's Survivors' right to sell or transfer the Shares may be restricted; and

B. The Participant or the Participant's Survivors may be required to execute letters of investment intent and must also acknowledge that the Shares will bear legends noting any applicable restrictions.

(v) Term of Option: Each Option shall terminate not more than ten years from the date of the grant or at such earlier time as the Option Agreement may provide.

7. TERMS AND CONDITIONS OF STOCK GRANTS.

Each Stock Grant to a Participant shall state the principal terms in an Agreement duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Agreement shall be in a form approved by the Administrator and shall contain terms and conditions which the Administrator determines to be appropriate and in the best interest of the Company, subject to the following minimum standards:

(a) Each Agreement shall state the purchase price per share, if any, of the Shares covered by each Stock Grant, which purchase price shall be determined by the Administrator but shall not be less than the minimum consideration required by the Delaware General Corporation Law, if any, on the date of the grant of the Stock Grant;

(b) Each Agreement shall state the number of Shares to which the Stock Grant pertains; and

(c) Each Agreement shall include the terms of any right of the Company to restrict or reacquire the Shares subject to the Stock Grant, including the time and events upon which such rights shall accrue and the purchase price therefor, if any.

(d) Dividends (other than stock dividends to be issued pursuant to Section 24 of the Plan) may accrue but shall not be paid prior to the time, and only to the extent that, the restrictions or rights to reacquire the Shares subject to the Stock Grant lapse.

8. TERMS AND CONDITIONS OF OTHER STOCK-BASED AWARDS.

The Administrator shall have the right to grant other Stock-Based Awards based upon the Common Stock having such terms and conditions as the Administrator may determine, including, without limitation, the grant of Shares based upon certain conditions, the grant of securities convertible into Shares and the grant of stock appreciation rights, phantom stock awards or stock units. The principal terms of each Stock-Based Award shall be set forth in an Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Agreement shall be in a form approved by the Administrator

and shall contain terms and conditions which the Administrator determines to be appropriate and in the best interest of the Company. Each Agreement shall include the terms of any right of the Company including the right to terminate the Stock-Based Award without the issuance of Shares, the terms of any vesting conditions or events upon which Shares shall be issued; provided that dividends (other than stock dividends to be issued pursuant to Section 24 of the Plan) or dividend equivalents may accrue but shall not be paid prior to and only to the extent that, the Shares subject to the Stock-Based Award vest. Under no circumstances may the Agreement covering stock appreciation rights (a) have an exercise price (per share) that is less than the Fair Market Value per share of Common Stock on the date of grant or (b) expire more than ten years following the date of grant. The Company intends that the Plan and any Stock-Based Awards granted hereunder be exempt from the application of Section 409A of the Code or meet the requirements of paragraphs (2), (3) and (4) of subsection (a) of Section 409A of the Code, to the extent applicable, and be operated in accordance with Section 409A so that any compensation deferred under any Stock-Based Award (and applicable investment earnings) shall not be included in income under Section 409A of the Code. Any ambiguities in the Plan shall be construed to effect the intent as described in this Paragraph 8.

9. EXERCISE OF OPTIONS AND ISSUE OF SHARES.

An Option (or any part or installment thereof) shall be exercised by giving written notice to the Company or its designee (in a form acceptable to the Administrator, which may include electronic notice), together with provision for payment of the aggregate exercise price in accordance with this Paragraph for the Shares as to which the Option is being exercised, and upon compliance with any other condition(s) set forth in the Option Agreement. Such notice shall be signed by the person exercising the Option (which signature may be provided electronically in a form acceptable to the Administrator), shall state the number of Shares with respect to which the Option is being exercised and shall contain any representation required by the Plan or the Option Agreement. Payment of the exercise price for the Shares as to which such Option is being exercised shall be made (a) in United States dollars in cash or by check, or (b) at the discretion of the Administrator, through delivery of shares of Common Stock held for at least six months (if required to avoid negative accounting treatment) having a Fair Market Value equal as of the date of the exercise to the aggregate cash exercise price for the number of Shares as to which the Option is being exercised, or (c) at the discretion of the Administrator, by having the Company retain from the Shares otherwise issuable upon exercise of the Option, a number of Shares having a Fair Market Value equal as of the date of exercise to the aggregate exercise price for the number of Shares as to which the Option is being exercised, or (d) at the discretion of the Administrator, in accordance with a cashless exercise program established with a securities brokerage firm, and approved by the Administrator, or (e) at the discretion of the Administrator, by any combination of (a), (b), (c) and (d) above or (f) at the discretion of the Administrator, by payment of such other lawful consideration as the Administrator may determine.

The Company shall then reasonably promptly deliver the Shares as to which such Option was exercised to the Participant (or to the Participant's Survivors, as the case may be). In determining what constitutes "reasonably promptly," it is expressly understood that the issuance and delivery of the Shares may be delayed by the Company in order to comply with any law or regulation (including, without limitation, state securities or "blue sky" laws) which requires the

Company to take any action with respect to the Shares prior to their issuance. The Shares shall, upon delivery, be fully paid, non-assessable Shares.

10. PAYMENT IN CONNECTION WITH THE ISSUANCE OF STOCK GRANTS AND STOCK-BASED AWARDS AND ISSUE OF SHARES.

Any Stock Grant or Stock-Based Award requiring payment of a purchase price for the Shares as to which such Stock Grant or Stock-Based Award is being granted shall be made (a) in United States dollars in cash or by check, or (b) at the discretion of the Administrator, through delivery of shares of Common Stock held for at least six months (if required to avoid negative accounting treatment)and having a Fair Market Value equal as of the date of payment to the purchase price of the Stock Grant or Stock-Based Award, or (c) at the discretion of the Administrator, by any combination of (a) and (b) above; or (d) at the discretion of the Administrator, by payment of such other lawful consideration as the Administrator may determine.

The Company shall, when required by the applicable Agreement, reasonably promptly deliver the Shares as to which such Stock Grant or Stock-Based Award was made to the Participant (or to the Participant's Survivors, as the case may be), subject to any escrow provision set forth in the applicable Agreement. In determining what constitutes "reasonably promptly," it is expressly understood that the issuance and delivery of the Shares may be delayed by the Company in order to comply with any law or regulation (including, without limitation, state securities or "blue sky" laws) which requires the Company to take any action with respect to the Shares prior to their issuance.

11. RIGHTS AS A SHAREHOLDER.

No Participant to whom a Stock Right has been granted shall have rights as a shareholder with respect to any Shares covered by such Stock Right except after due exercise of an Option or issuance of Shares as set forth in any Agreement, tender of the aggregate exercise or purchase price, if any, for the Shares being purchased and registration of the Shares in the Company's share register in the name of the Participant.

12. ASSIGNABILITY AND TRANSFERABILITY OF STOCK RIGHTS.

By its terms, a Stock Right granted to a Participant shall not be transferable by the Participant other than (i) by will or by the laws of descent and distribution, or (ii) as approved by the Administrator in its discretion and set forth in the applicable Agreement provided that no Stock Right may be transferred by a Participant for value. The designation of a beneficiary of a Stock Right by a Participant, with the prior approval of the Administrator and in such form as the Administrator shall prescribe, shall not be deemed a transfer prohibited by this Paragraph. Except as provided above during the Participant's lifetime a Stock Right shall only be exercisable by or issued to such Participant (or his or her legal representative) and shall not be assigned, pledged or hypothecated in any way (whether by operation of law or otherwise) and shall not be subject to execution, attachment or similar process. Any attempted transfer, assignment, pledge, hypothecation or other disposition of any Stock Right or of any rights

granted thereunder contrary to the provisions of this Plan, or the levy of any attachment or similar process upon a Stock Right, shall be null and void.

13. EFFECT ON OPTIONS OF TERMINATION OF SERVICE OTHER THAN FOR CAUSE OR DEATH OR DISABILITY.

Except as otherwise provided in a Participant's Option Agreement, in the event of a termination of service with the Company or an Affiliate before the Participant has exercised an Option, the following rules apply:

(a) A Participant who ceases to provide services to the Company or an Affiliate (for any reason other than termination for Cause, Disability, or death for which events there are special rules in Paragraphs 14, 15, and 16, respectively), may exercise any Option granted to him or her to the extent that the Option is exercisable on the date of such termination of service, but only within such term as the Administrator has designated in a Participant's Option Agreement.

(b) The provisions of this Paragraph, and not the provisions of Paragraph 15 or 16, shall apply to a Participant who subsequently becomes Disabled or dies after the termination of service; provided, however, in the case of a Participant's Disability or death within three months after the termination of service, the Participant or the Participant's Survivors may exercise the Option within one year after the date of the Participant's termination of service, but in no event after the date of expiration of the term of the Option.

(c) Notwithstanding anything herein to the contrary, if subsequent to a Participant's termination of service, but prior to the exercise of an Option, the Administrator or the Board of Directors determines that, either prior or subsequent to the Participant's termination, the Participant engaged in conduct which would constitute Cause, then such Participant shall forthwith cease to have any right to exercise any Option.

(d) A Participant to whom an Option has been granted under the Plan who is absent from the Company or an Affiliate because of temporary disability (any disability other than a Disability as defined in Paragraph 1 hereof), or who is on leave of absence for any purpose, shall not, during the period of any such absence, be deemed, by virtue of such absence alone, to have terminated such Participant's service with the Company or with an Affiliate, except as the Administrator may otherwise expressly provide.

(e) Except as required by law or as set forth in a Participant's Option Agreement, Options granted under the Plan shall not be affected by any change of a Participant's status within or among the Company and any Affiliates, so long as the Participant continues to be an Employee or Consultant of the Company or any Affiliate.

14. EFFECT ON OPTIONS OF TERMINATION OF SERVICE FOR CAUSE.

Except as otherwise provided in a Participant's Option Agreement, the following rules apply if the Participant's service with the Company or an Affiliate is terminated for Cause prior to the time that all of his or her outstanding Options have been exercised:

(a) All outstanding and unexercised Options as of the time the Participant is notified his or her service is terminated for Cause will immediately be forfeited.

(b) Cause is not limited to events which have occurred prior to a Participant's termination of service, nor is it necessary that the Administrator's finding of Cause occur prior to termination. If the Administrator determines, subsequent to a Participant's termination of service but prior to the exercise of an Option, that either prior or subsequent to the Participant's termination the Participant engaged in conduct which would constitute Cause, then the right to exercise any Option is forfeited.

15. EFFECT ON OPTIONS OF TERMINATION OF SERVICE FOR DISABILITY.

Except as otherwise provided in a Participant's Option Agreement,

(a) A Participant who ceases to be an Employee of the Company or of an Affiliate by reason of Disability may exercise any Option granted to such Participant:

(i) To the extent that the Option has become exercisable but has not been exercised on the date of the Participant's termination of service due to Disability; and

(ii) In the event rights to exercise the Option accrue periodically, to the extent of a pro rata portion through the date of the Participant's termination of service due to Disability of any additional vesting rights that would have accrued on the next vesting date had the Participant not become Disabled. The proration shall be based upon the number of days accrued in the current vesting period prior to the date of the Participant's termination of service due to Disability.

(b) A Disabled Participant may exercise the Option only within the period ending one year after the date of the Participant's termination of service due to Disability, notwithstanding that the Participant might have been able to exercise the Option as to some or all of the Shares on a later date if the Participant had not been terminated due to Disability and had continued to be an Employee or, if earlier, within the originally prescribed term of the Option. The Administrator shall make the determination both of whether Disability has occurred and the date of its occurrence (unless a procedure for such determination is set forth in another agreement between the Company and such Participant, in which case such procedure shall be used for such determination). If requested, the Participant shall be examined by a physician selected or approved by the Administrator, the cost of which examination shall be paid for by the Company.

16. EFFECT ON OPTIONS OF DEATH WHILE AN EMPLOYEE.

Except as otherwise provided in a Participant's Option Agreement,

(a) In the event of the death of a Participant while the Participant is an Employee of the Company or of an Affiliate, such Option may be exercised by the Participant's Survivors:

(i) To the extent that the Option has become exercisable but has not been exercised on the date of death; and

(ii) In the event rights to exercise the Option accrue periodically, to the extent of a pro rata portion through the date of death of any additional vesting rights that would have accrued on the next vesting date had the Participant not died. The proration shall be based upon the number of days accrued in the current vesting period prior to the Participant's date of death.

(b) If the Participant's Survivors wish to exercise the Option, they must take all necessary steps to exercise the Option within one year after the date of death of such Participant, notwithstanding that the decedent might have been able to exercise the Option as to some or all of the Shares on a later date if he or she had not died and had continued to be an Employee or, if earlier, within the originally prescribed term of the Option.

17. EFFECT OF TERMINATION OF SERVICE ON STOCK GRANTS AND STOCK-BASED AWARDS.

In the event of a termination of service as an Employee with the Company or an Affiliate for any reason before the Participant has accepted a Stock Grant or a Stock-Based Award and paid the purchase price, if required at the time, such grant shall terminate.

For purposes of this Paragraph 17 and Paragraph 18 below, a Participant to whom a Stock Grant or a Stock-Based Award has been issued under the Plan who is absent from work with the Company or with an Affiliate because of temporary disability (any disability other than a Disability as defined in Paragraph 1 hereof), or who is on leave of absence for any purpose, shall not, during the period of any such absence, be deemed, by virtue of such absence alone, to have terminated such Participant's employment with the Company or with an Affiliate, except as the Administrator may otherwise expressly provide.

In addition, for purposes of this Paragraph 17 and Paragraph 18 below, any change of employment or other service within or among the Company and any Affiliates shall not be treated as a termination of employment, so long as the Participant continues to be an Employee or Consultant of the Company or any Affiliate.

18. EFFECT ON STOCK GRANTS AND STOCK-BASED AWARDS OF TERMINATION OF SERVICE OTHER THAN FOR CAUSE OR DEATH OR DISABILITY.

Except as otherwise provided in a Participant's Agreement, in the event of a termination of service, other than termination for Cause, death or Disability for which events there are special rules in Paragraphs 19, 20, and 21, respectively, before all forfeiture provisions or Company rights of repurchase (other than rights to repurchase at then fair market value following termination of service) shall have lapsed, then the Company shall have the right to cancel or repurchase that number of Shares subject to a Stock Grant or Stock-Based Award as to which the Company's forfeiture or repurchase rights have not lapsed.

19. EFFECT ON STOCK GRANTS AND STOCK-BASED AWARDS OF TERMINATION OF SERVICE FOR CAUSE.

Except as otherwise provided in a Participant's Agreement, the following rules apply if the Participant's service with the Company or an Affiliate is terminated for Cause:

(a) All Shares subject to any Stock Grant or Stock-Based Award that remain subject to forfeiture provisions or as to which the Company shall have a repurchase right shall be immediately forfeited to the Company as of the time the Participant is notified his or her service is terminated for Cause.

(b) Cause is not limited to events which have occurred prior to a Participant's termination of service, nor is it necessary that the Administrator's finding of Cause occur prior to termination. If the Administrator determines, subsequent to a Participant's termination of service, that either prior or subsequent to the Participant's termination the Participant engaged in conduct which would constitute Cause, then all Shares subject to any Stock Grant or Stock-Based Award that remained subject to forfeiture provisions or as to which the Company had a repurchase right on the date of termination shall be immediately forfeited to the Company.

20. EFFECT ON STOCK GRANTS AND STOCK-BASED AWARDS OF TERMINATION OF SERVICE FOR DISABILITY.

Except as otherwise provided in a Participant's Agreement, the following rules apply if a Participant ceases to be an Employee of the Company or of an Affiliate by reason of Disability: to the extent the forfeiture provisions or the Company's rights of repurchase have not lapsed on the date of Disability, they shall be exercisable; provided, however, that in the event such forfeiture provisions or rights of repurchase lapse periodically, such provisions or rights shall lapse to the extent of a pro rata portion of the Shares subject to such Stock Grant or Stock-Based Award through the date of Disability as would have lapsed had the Participant not become Disabled. The proration shall be based upon the number of days accrued prior to the date of Disability.

The Administrator shall make the determination both as to whether Disability has occurred and the date of its occurrence (unless a procedure for such determination is set forth in another agreement between the Company and such Participant, in which case such procedure shall be used for such determination). If requested, the Participant shall be examined by a physician selected or approved by the Administrator, the cost of which examination shall be paid for by the Company.

21. EFFECT ON STOCK GRANTS AND STOCK-BASED AWARDS OF DEATH WHILE AN EMPLOYEE.

Except as otherwise provided in a Participant's Agreement, the following rules apply in the event of the death of a Participant while the Participant is an Employee of the Company or of an Affiliate: to the extent the forfeiture provisions or the Company's rights of repurchase have not lapsed on the date of death, they shall be exercisable; provided, however, that in the event such forfeiture provisions or rights of repurchase lapse periodically, such provisions or rights shall lapse to the extent of a pro rata portion of the Shares subject to such Stock Grant or Stock-Based Award through the date of death as would have lapsed had the Participant not died. The proration shall be based upon the number of days accrued prior to the Participant's date of death.

22. PURCHASE FOR INVESTMENT.

Unless the offering and sale of the Shares shall have been effectively registered under the Securities Act, the Company shall be under no obligation to issue Shares under the Plan unless and until the following conditions have been fulfilled:

(a) The person who receives a Stock Right shall warrant to the Company, prior to the receipt of Shares, that such person is acquiring such Shares for his or her own account, for investment, and not with a view to, or for sale in connection with, the distribution of any such Shares, in which event the person acquiring such Shares shall be bound by the provisions of the following legend (or a legend in substantially similar form) which shall be endorsed upon the certificate evidencing the Shares issued pursuant to such exercise or such grant:

> "The shares represented by this certificate have been taken for investment and they may not be sold or otherwise transferred by any person, including a pledgee, unless (1) either (a) a Registration Statement with respect to such shares shall be effective under the Securities Act of 1933, as amended, or (b) the Company shall have received an opinion of counsel satisfactory to it that an exemption from registration under such Act is then available, and (2) there shall have been compliance with all applicable state securities laws."

(b) At the discretion of the Administrator, the Company shall have received an opinion of its counsel that the Shares may be issued in compliance with the Securities Act without registration thereunder.

23. DISSOLUTION OR LIQUIDATION OF THE COMPANY.

Upon the dissolution or liquidation of the Company, all Options granted under this Plan which as of such date shall not have been exercised and all Stock Grants and Stock-Based Awards which have not been accepted, to the extent required under the applicable Agreement, will terminate and become null and void; provided, however, that if the rights of a Participant or a Participant's Survivors have not otherwise terminated and expired, the Participant or the Participant's Survivors will have the right immediately prior to such dissolution or liquidation to exercise or accept any Stock Right to the extent that the Stock Right is exercisable or subject to acceptance as of the date immediately prior to such dissolution or liquidation. Upon the dissolution or liquidation of the Company, any outstanding Stock-Based Awards shall immediately terminate unless otherwise determined by the Administrator or specifically provided in the applicable Agreement.

24. ADJUSTMENTS.

Upon the occurrence of any of the following events, a Participant's rights with respect to any Stock Right granted to him or her hereunder shall be adjusted as hereinafter provided, unless otherwise specifically provided in a Participant's Agreement:

(a) Stock Dividends and Stock Splits. If (i) the shares of Common Stock shall be subdivided or combined into a greater or smaller number of shares or if the Company shall issue any shares of Common Stock as a stock dividend on its outstanding Common Stock, or (ii)

additional shares or new or different shares or other securities of the Company or other non-cash assets are distributed with respect to such shares of Common Stock, each Stock Right and the number of shares of Common Stock deliverable thereunder shall be appropriately increased or decreased proportionately, and appropriate adjustments shall be made including, in the exercise or purchase price per share, to reflect such events. The number of Shares subject to the limitations in Paragraph 3(a), 3(b) and 4(c) shall also be proportionately adjusted upon the occurrence of such events.

(b) Corporate Transactions. If the Company is to be consolidated with or acquired by another entity in a merger, consolidation, sale of all or substantially all of the Company's assets or the acquisition of all of the outstanding voting stock of the Company in a single transaction or a series of related transactions other than a transaction to merely change the state of incorporation (a "Corporate Transaction"), the Administrator or the board of directors of any entity assuming the obligations of the Company hereunder (the "Successor Board"), shall, as to outstanding Options, either (i) make appropriate provision for the continuation of such Options by substituting on an equitable basis for the Shares then subject to such Options either the consideration payable with respect to the outstanding shares of Common Stock in connection with the Corporate Transaction or securities of any successor or acquiring entity; or (ii) upon written notice to the Participants, provide that such Options must be exercised (either (A) to the extent then exercisable or, (B) at the discretion of the Administrator, any such Options being made partially or fully exercisable for purposes of this Subparagraph), within a specified number of days of the date of such notice, at the end of which period such Options which have not been exercised shall terminate; or (iii) terminate such Options in exchange for payment of an amount equal to the consideration payable upon consummation of such Corporate Transaction to a holder of the number of shares of Common Stock into which such Option would have been exercisable (either (A) to the extent then exercisable or, (B) at the discretion of the Administrator, any such Options being made partially or fully exercisable for purposes of this Subparagraph) less the aggregate exercise price thereof. For purposes of determining the payments to be made pursuant to Subclause (iii) above, in the case of a Corporate Transaction the consideration for which, in whole or in part, is other than cash, the consideration other than cash shall be valued at the fair value thereof as determined in good faith by the Board of Directors.

With respect to outstanding Stock Grants, the Administrator or the Successor Board, shall make appropriate provision for the continuation of such Stock Grants on the same terms and conditions by substituting on an equitable basis for the Shares then subject to such Stock Grants either the consideration payable with respect to the outstanding Shares of Common Stock in connection with the Corporate Transaction or securities of any successor or acquiring entity. In lieu of the foregoing, in connection with any Corporate Transaction, the Administrator may provide that, upon consummation of the Corporate Transaction, each outstanding Stock Grant shall be terminated in exchange for payment of an amount equal to the consideration payable upon consummation of such Corporate Transaction to a holder of the number of shares of Common Stock comprising such Stock Grant (to the extent such Stock Grant is no longer subject to any forfeiture or repurchase rights then in effect or, at the discretion of the Administrator, all forfeiture and repurchase rights being waived upon such Corporate Transaction). For purposes of determining such payments, in the case of a Corporate Transaction the consideration for which, in whole or in part, is other than cash, the consideration other than cash shall be valued at the fair value thereof as determined in good faith by the Board of Directors.

In taking any of the actions permitted under this Paragraph 24(b), the Administrator shall not be obligated by the Plan to treat all Stock Rights, all Stock Rights held by a Participant, or all Stock Rights of the same type, identically.

(c) Recapitalization or Reorganization. In the event of a recapitalization or reorganization of the Company other than a Corporate Transaction pursuant to which securities of the Company or of another corporation, limited liability company or other entity are issued with respect to the outstanding shares of Common Stock, a Participant upon exercising an Option or accepting a Stock Grant after the recapitalization or reorganization shall be entitled to receive for the price paid upon such exercise or acceptance if any, the number of replacement securities which would have been received if such Option had been exercised or Stock Grant accepted prior to such recapitalization or reorganization.

(d) Adjustments to Stock-Based Awards. Upon the happening of any of the events described in Subparagraphs (a), (b) or (c) above, any outstanding Stock-Based Award shall be appropriately adjusted to reflect the events described in such Subparagraphs. The Administrator or the Successor board shall determine the specific adjustments to be made under Paragraph 24, including, but not limited to, the effect of any Corporate Transaction and, subject to Paragraph 4, its determination shall be conclusive.

(e) Modification of Options. Notwithstanding the foregoing, any adjustments made pursuant to Subparagraph (a), (b) or (c) above with respect to Options shall be made only after the Administrator determines whether such adjustments would cause any adverse tax consequences for the holders of Options, including, but not limited to, pursuant to Section 409A of the Code. If the Administrator determines that such adjustments made with respect to Options would constitute a modification or other adverse tax consequence, it may in its discretion refrain from making such adjustments, unless the holder of an Option specifically agrees in writing that such adjustment be made and such writing indicates that the holder has full knowledge of the consequences of such "modification" on his or her income tax treatment with respect to the Option.

25. ISSUANCES OF SECURITIES.

Except as expressly provided herein, no issuance by the Company of shares of stock of any class, or securities convertible into shares of stock of any class, shall affect, and no adjustment by reason thereof shall be made with respect to, the number or price of shares subject to Stock Rights. Except as expressly provided herein, no adjustments shall be made for dividends paid in cash or in property (including without limitation, securities) of the Company prior to any issuance of Shares pursuant to a Stock Right.

26. FRACTIONAL SHARES.

No fractional shares shall be issued under the Plan and the person exercising a Stock Right shall receive from the Company cash in lieu of such fractional shares equal to the Fair Market Value thereof.

27. WITHHOLDING.

In the event that any federal, state, or local income taxes, employment taxes, Federal Insurance Contributions Act ("F.I.C.A.") withholdings or other amounts are required by applicable law or governmental regulation to be withheld from the Participant's salary, wages or other remuneration in connection with the issuance of a Stock Right or Shares under the Plan or upon the lapsing of any forfeiture provision or right of repurchase or for any other reason required by law, the Company may withhold from the Participant's compensation, if any, or may require that the Participant advance in cash to the Company, or to any Affiliate of the Company which employs or employed the Participant, the statutory minimum amount of such withholdings unless a different withholding arrangement, including the use of shares of the Company's Common Stock or a promissory note, is authorized by the Administrator (and permitted by law). For purposes hereof, the fair market value of the shares withheld for purposes of payroll withholding shall be determined in the manner set forth under the definition of Fair Market Value provided in Paragraph 1 above, as of the most recent practicable date prior to the date of exercise. If the Fair Market Value of the shares withheld is less than the amount of payroll withholdings required, the Participant may be required to advance the difference in cash to the Company or the Affiliate employer.

28. TERMINATION OF THE PLAN.

The Plan will terminate on March 11, 2029, the date which is ten years from the date of its adoption by the Board of Directors. The Plan may be terminated at an earlier date by vote of the Board of Directors of the Company; provided, however, that any such earlier termination shall not affect any Agreements executed prior to the effective date of such termination. Termination of the Plan shall not affect any Stock Rights theretofore granted.

29. AMENDMENT OF THE PLAN AND AGREEMENTS.

The Plan may be amended by the Board of Directors of the Company. The Plan may also be amended by the Administrator, including, without limitation, to the extent necessary to qualify the Shares issuable under the Plan for listing on any national securities exchange or quotation in any national automated quotation system of securities dealers. Any amendment approved by the Administrator which the Administrator determines is of a scope that requires shareholder approval shall be subject to obtaining such shareholder approval. Any modification or amendment of the Plan shall not, without the consent of a Participant, adversely affect his or her rights under a Stock Right previously granted to him or her. With the consent of the Participant affected, the Administrator may amend outstanding Agreements in a manner which may be adverse to the Participant but which is not inconsistent with the Plan. In the discretion of the Administrator, outstanding Agreements may be amended by the Administrator in a manner which is not adverse to the Participant. Nothing in this Paragraph 29 shall limit the Administrator's authority to take any action permitted pursuant to Paragraph 24.

30. EMPLOYMENT OR OTHER RELATIONSHIP.

Nothing in this Plan or any Agreement shall be deemed to prevent the Company or an Affiliate from terminating the employment of a Participant, nor to prevent a Participant from

terminating his or her own employment, or to give any Participant a right to be retained in employment or other service by the Company or any Affiliate for any period of time.

31. SECTION 409A.

If a Participant is a "specified employee" as defined in Section 409A of the Code (and as applied according to procedures of the Company and its Affiliates) as of his separation from service, to the extent any payment under this Plan or pursuant to the grant of a Stock-Based Award constitutes deferred compensation (after taking into account any applicable exemptions from Section 409A of the Code), and to the extent required by Section 409A of the Code, no payments due under this Plan or pursuant to a Stock-Based Award may be made until the earlier of: (i) the first day of the seventh month following the Participant's separation from service, or (ii) the Participant's date of death; provided, however, that any payments delayed during this six-month period shall be paid in the aggregate in a lump sum, without interest, on the first day of the seventh month following the Participant's separation from service.

The Administrator shall administer the Plan with a view toward ensuring that Stock Rights under the Plan that are subject to Section 409A of the Code comply with the requirements thereof and that Options under the Plan be exempt from the requirements of Section 409A of the Code, but neither the Administrator nor any member of the Board, nor the Company nor any of its Affiliates, nor any other person acting hereunder on behalf of the Company, the Administrator or the Board shall be liable to a Participant or any Survivor by reason of the acceleration of any income, or the imposition of any additional tax or penalty, with respect to a Stock Right, whether by reason of a failure to satisfy the requirements of Section 409A of the Code or otherwise.

32. INDEMNITY.

Neither the Board nor the Administrator, nor any members of either, nor any employees of the Company or any parent, subsidiary, or other Affiliate, shall be liable for any act, omission, interpretation, construction or determination made in good faith in connection with their responsibilities with respect to this Plan, and the Company hereby agrees to indemnify the members of the Board, the members of the Committee, and the employees of the Company and its parent or subsidiaries in respect of any claim, loss, damage, or expense (including reasonable counsel fees) arising from any such act, omission, interpretation, construction or determination to the full extent permitted by law.

33. CLAWBACK.

Notwithstanding anything to the contrary contained in this Plan, the Company may recover from a Participant any compensation received from any Stock Right (whether or not settled) or cause a Participant to forfeit any Stock Right (whether or not vested) in the event that the Company's Clawback Policy then in effect is triggered.

34. GOVERNING LAW.

This Plan shall be construed and enforced in accordance with the law of the State of Delaware.

Exhibit 10.4
Option No. _____

SPERO THERAPEUTICS, INC.

Stock Option Grant Notice

Stock Option Grant under the Company's
2019 Inducement Equity Incentive Plan

1. Name and Address of Participant:

2. Date of Option Grant:

3. Type of Grant:Non-Qualified Stock Option

4. Maximum Number of Shares for which this Option is exercisable:

5. Exercise (purchase) price per share:

6. Option Expiration Date:

7. Vesting Start Date:

8. Vesting Schedule: This Option shall become exercisable (and the Shares issued upon exercise shall be vested) as follows provided the Participant is an Employee of the Company or of an Affiliate on the applicable vesting date:

   [25% of the Shares shall be vested on the first anniversary of the Vesting Start Date, and thereafter the remainder of the Shares not yet vested shall vest in equal monthly installments for 36 months beginning on the first anniversary of the Vesting Start Date.]

The foregoing rights are cumulative and are subject to the other terms and conditions of this Agreement.

The Company and the Participant acknowledge receipt of this Stock Option Grant Notice and agree to the terms of the Stock Option Agreement attached hereto and incorporated by reference herein and the Company's 2019 Inducement Equity Incentive Plan.

SPERO THERAPEUTICS, INC.

By:
Name:
Title:

Participant

SPERO THERAPEUTICS, INC.

STOCK OPTION AGREEMENT—INCORPORATED TERMS AND CONDITIONS

(Non-Qualified Stock Option)

AGREEMENT made as of the date of grant set forth in the Stock Option Grant Notice by and between Spero Therapeutics, Inc. (the "***Company***"), a Delaware corporation, and the individual whose name appears on the Stock Option Grant Notice (the "***Participant***").

WHEREAS, the Company desires to grant to the Participant an option (the "***Option***") to purchase shares of its common stock, $0.001 par value per share (the "***Shares***"), under and for the purposes set forth in the Company's 2019 Inducement Equity Incentive Plan (the "***Plan***");

WHEREAS, the Company and the Participant understand and agree that the Option shall be granted in compliance with Nasdaq Listing Rule 5635(c)(4) as a material inducement to the Participant entering into employment with the Company;

WHEREAS, the Company and the Participant understand and agree that any terms used and not defined herein have the same meanings as in the Plan; and

WHEREAS, the Company and the Participant each intend that the Option granted herein shall be of the type set forth in the Stock Option Grant Notice.

NOW, THEREFORE, in consideration of the mutual covenants hereinafter set forth and for other good and valuable consideration, the parties hereto agree as follows:

1. GRANT OF OPTION.

The Company hereby grants to the Participant the right and option to purchase all or any part of an aggregate of the number of Shares set forth in the Stock Option Grant Notice, on the terms and conditions and subject to all the limitations set forth herein, under United States securities and tax laws, and in the Plan, which is incorporated herein by reference. The Participant acknowledges receipt of a copy of the Plan.

2. EXERCISE PRICE.

The exercise price of the Shares covered by the Option shall be the amount per Share set forth in the Stock Option Grant Notice, subject to adjustment, as provided in the Plan, in the event of a stock split, reverse stock split or other events affecting the holders of Shares after the date hereof (the "***Exercise Price***"). Payment shall be made in accordance with Paragraph 9 of the Plan.

3. EXERCISABILITY OF OPTION.

Subject to the terms and conditions set forth in this Agreement and the Plan, the Option granted hereby shall become vested and exercisable as set forth in the Stock Option Grant Notice and is subject to the other terms and conditions of this Agreement and the Plan.

4. TERM OF OPTION.

This Option shall terminate on the Option Expiration Date as specified in the Stock Option Grant Notice, but shall be subject to earlier termination as provided herein or in the Plan.

If the Participant ceases to be an Employee of the Company or of an Affiliate for any reason other than the death or Disability of the Participant, or termination of the Participant for Cause (the "***Termination Date***"), the Option to the extent then vested and exercisable pursuant to Section 3 hereof as of the Termination Date, and not previously

terminated in accordance with this Agreement, may be exercised within three months after the Termination Date, or on or prior to the Option Expiration Date as specified in the Stock Option Grant Notice, whichever is earlier, but may not be exercised thereafter except as set forth below. In such event, the unvested portion of the Option shall not be exercisable and shall expire and be cancelled on the Termination Date.

If the Participant ceases to be an Employee of the Company or of an Affiliate but continues after termination of employment to provide service to the Company or an Affiliate as a Consultant, this Option shall continue to vest in accordance with Section 3 above as if this Option had not terminated until the Participant is no longer providing services to the Company. In such case, this Option shall continue on the same terms and conditions set forth herein until such Participant is no longer providing service to the Company or an Affiliate.

Notwithstanding the foregoing, in the event of the Participant's Disability or death within three months after the Termination Date, the Participant or the Participant's Survivors may exercise the Option within one year after the Termination Date, but in no event after the Option Expiration Date as specified in the Stock Option Grant Notice.

In the event the Participant's service is terminated by the Company or an Affiliate for Cause, the Participant's right to exercise any unexercised portion of this Option even if vested shall cease immediately as of the time the Participant is notified his or her service is terminated for Cause, and this Option shall thereupon terminate. Notwithstanding anything herein to the contrary, if subsequent to the Participant's termination, but prior to the exercise of the Option, the Administrator determines that, either prior or subsequent to the Participant's termination, the Participant engaged in conduct which would constitute Cause, then the Participant shall immediately cease to have any right to exercise the Option and this Option shall thereupon terminate.

In the event of the Disability of the Participant, as determined in accordance with the Plan, the Option shall be exercisable within one year after the Participant's termination of service due to Disability or, if earlier, on or prior to the Option Expiration Date as specified in the Stock Option Grant Notice. In such event, the Option shall be exercisable:

(a) to the extent that the Option has become exercisable but has not been exercised as of the date of the Participant's termination of service due to Disability; and

(b) in the event rights to exercise the Option accrue periodically, to the extent of a pro rata portion through the date of the Participant's termination of service due to Disability of any additional vesting rights that would have accrued on the next vesting date had the Participant not become Disabled. The proration shall be based upon the number of days accrued in the current vesting period prior to the date of the Participant's termination of service due to Disability.

In the event of the death of the Participant while an Employee of the Company or of an Affiliate, the Option shall be exercisable by the Participant's Survivors within one year after the date of death of the Participant or, if earlier, on or prior to the Option Expiration Date as specified in the Stock Option Grant Notice. In such event, the Option shall be exercisable:

(x) to the extent that the Option has become exercisable but has not been exercised as of the date of death; and

(y) in the event rights to exercise the Option accrue periodically, to the extent of a pro rata portion through the date of death of any additional vesting rights that would have accrued on the next vesting date had the Participant not died. The proration shall be based upon the number of days accrued in the current vesting period prior to the Participant's date of death.

5. METHOD OF EXERCISING OPTION.

Subject to the terms and conditions of this Agreement, the Option may be exercised by written notice to the Company or its designee, in substantially the form of Exhibit A attached hereto (or in such other form acceptable to

the Company, which may include electronic notice). Such notice shall state the number of Shares with respect to which the Option is being exercised and shall be signed by the person exercising the Option (which signature may be provided electronically in a form acceptable to the Company). Payment of the Exercise Price for such Shares shall be made in accordance with Paragraph 9 of the Plan. The Company shall deliver such Shares as soon as practicable after the notice shall be received, provided, however, that the Company may delay issuance of such Shares until completion of any action or obtaining of any consent, which the Company deems necessary under any applicable law (including, without limitation, state securities or "blue sky" laws). The Shares as to which the Option shall have been so exercised shall be registered in the Company's share register in the name of the person so exercising the Option (or, if the Option shall be exercised by the Participant and if the Participant shall so request in the notice exercising the Option, shall be registered in the Company's share register in the name of the Participant and another person jointly, with right of survivorship) and shall be delivered as provided above to or upon the written order of the person exercising the Option. In the event the Option shall be exercised, pursuant to Section 4 hereof, by any person other than the Participant, such notice shall be accompanied by appropriate proof of the right of such person to exercise the Option. All Shares that shall be purchased upon the exercise of the Option as provided herein shall be fully paid and nonassessable.

6. PARTIAL EXERCISE.

Exercise of this Option to the extent above stated may be made in part at any time and from time to time within the above limits, except that no fractional share shall be issued pursuant to this Option.

7. NON-ASSIGNABILITY.

The Option shall not be transferable by the Participant otherwise than (i) by will, (ii) by the laws of descent and distribution, (iii) pursuant to a qualified domestic relations order as defined by the Code or Title I of the Employee Retirement Income Security Act or the rules thereunder, or (iv) for no consideration to or for the benefit of the Participant's Immediate Family (including, without limitation, to a trust for the benefit of the Participant's Immediate Family or to a partnership or limited liability company for one or more members of the Participant's Immediate Family), and the transferee shall remain subject to all the terms and conditions applicable to the Option prior to such transfer and each such transferee shall so acknowledge in writing as a condition precedent to the effectiveness of such transfer. The term "***Immediate Family***" shall mean the Participant's spouse, former spouse, parents, children, stepchildren, adoptive relationships, sisters, brothers, nieces, nephews and grandchildren (and, for this purpose, shall also include the Participant). Except as provided above in this paragraph, the Option shall be exercisable, during the Participant's lifetime, only by the Participant (or, in the event of legal incapacity or incompetency, by the Participant's guardian or representative) and shall not be assigned, pledged or hypothecated in any way (whether by operation of law or otherwise) and shall not be subject to execution, attachment or similar process. Any attempted transfer, assignment, pledge, hypothecation or other disposition of the Option or of any rights granted hereunder contrary to the provisions of this Section 7, or the levy of any attachment or similar process upon the Option shall be null and void.

8. NO RIGHTS AS STOCKHOLDER UNTIL EXERCISE.

The Participant shall have no rights as a stockholder with respect to Shares subject to this Agreement until registration of the Shares in the Company's share register in the name of the Participant. Except as is expressly provided in the Plan with respect to certain changes in the capitalization of the Company, no adjustment shall be made for dividends or similar rights for which the record date is prior to the date of such registration.

9. ADJUSTMENTS.

The Plan contains provisions covering the treatment of Options in a number of contingencies such as stock splits and mergers. Provisions in the Plan for adjustment with respect to stock subject to Options and the related provisions with respect to successors to the business of the Company are hereby made applicable hereunder and are incorporated herein by reference.

10. TAXES.

The Participant acknowledges and agrees that (i) any income or other taxes due from the Participant with respect to this Option or the Shares issuable upon exercise of this Option shall be the Participant's responsibility; (ii) the Participant was free to use professional advisors of his or her choice in connection with this Agreement, has received advice from his or her professional advisors in connection with this Agreement, understands its meaning and import, and is entering into this Agreement freely and without coercion or duress; (iii) the Participant has not received and is not relying upon any advice, representations or assurances made by or on behalf of the Company or any Affiliate or any employee of or counsel to the Company or any Affiliate regarding any tax or other effects or implications of the Option, the Shares or other matters contemplated by this Agreement; and (iv) neither the Administrator, the Company, its Affiliates, nor any of its officers or directors, shall be held liable for any applicable costs, taxes, or penalties associated with the Option if, in fact, the Internal Revenue Service were to determine that the Option constitutes deferred compensation under Section 409A of the Code.

The Participant agrees that the Company may withhold from the Participant's remuneration, if any, the minimum statutory amount of federal, state and local withholding taxes attributable to such amount that is considered compensation includable in such person's gross income. At the Company's discretion, the amount required to be withheld may be withheld in cash from such remuneration, or in kind from the Shares otherwise deliverable to the Participant on exercise of the Option. The Participant further agrees that, if the Company does not withhold an amount from the Participant's remuneration sufficient to satisfy the Company's income tax withholding obligation, the Participant will reimburse the Company on demand, in cash, for the amount under-withheld.

11. PURCHASE FOR INVESTMENT.

Unless the offering and sale of the Shares to be issued upon the particular exercise of the Option shall have been effectively registered under the Securities Act, the Company shall be under no obligation to issue the Shares covered by such exercise unless the Company has determined that such exercise and issuance would be exempt from the registration requirements of the Securities Act and until the following conditions have been fulfilled:

(a) The person(s) who exercise the Option shall warrant to the Company, at the time of such exercise, that such person(s) are acquiring such Shares for their own respective accounts, for investment, and not with a view to, or for sale in connection with, the distribution of any such Shares, in which event the person(s) acquiring such Shares shall be bound by the provisions of the following legend which shall be endorsed upon any certificate(s) evidencing the Shares issued pursuant to such exercise:

"The shares represented by this certificate have been taken for investment and they may not be sold or otherwise transferred by any person, including a pledgee, unless (1) either (a) a Registration Statement with respect to such shares shall be effective under the Securities Act of 1933, as amended, or (b) the Company shall have received an opinion of counsel satisfactory to it that an exemption from registration under such Act is then available, and (2) there shall have been compliance with all applicable state securities laws;" and

(b) If the Company so requires, the Company shall have received an opinion of its counsel that the Shares may be issued upon such particular exercise in compliance with the Securities Act without registration thereunder. Without limiting the generality of the foregoing, the Company may delay issuance of the Shares until completion of any action or obtaining of any consent, which the Company deems necessary under any applicable law (including without limitation state securities or "blue sky" laws).

12. RESTRICTIONS ON TRANSFER OF SHARES.

12.1 The Participant agrees that in the event the Company proposes to offer for sale to the public any of its equity securities and such Participant is requested by the Company and any underwriter engaged by the Company in connection with such offering to sign an agreement restricting the sale or other transfer of Shares, then it will promptly sign such agreement and will not transfer,

whether in privately negotiated transactions or to the public in open market transactions or otherwise, any Shares or other securities of the Company held by him or her during such period as is determined by the Company and the underwriters, not to exceed 180 days following the closing of the offering, plus such additional period of time as may be required to comply with FINRA rules or similar rules thereto promulgated by another regulatory authority (such period, the "**Lock-Up Period**"). Such agreement shall be in writing and in form and substance reasonably satisfactory to the Company and such underwriter and pursuant to customary and prevailing terms and conditions. Notwithstanding whether the Participant has signed such an agreement, the Company may impose stop-transfer instructions with respect to the Shares or other securities of the Company subject to the foregoing restrictions until the end of the Lock-Up Period.

12.2 The Participant acknowledges and agrees that neither the Company, its stockholders nor its directors and officers, has any duty or obligation to disclose to the Participant any material information regarding the business of the Company or affecting the value of the Shares before, at the time of, or following a termination of the service of the Participant by the Company, including, without limitation, any information concerning plans for the Company to make a public offering of its securities or to be acquired by or merged with or into another firm or entity.

13. NO OBLIGATION TO MAINTAIN RELATIONSHIP.

The Participant acknowledges that: (i) the Company is not by the Plan or this Option Agreement obligated to continue the Participant as an employee or consultant of the Company or an Affiliate; (ii) the Plan is discretionary in nature and may be suspended or terminated by the Company at any time; (iii) the grant of the Option is a one-time benefit which does not create any contractual or other right to receive future grants of options, or benefits in lieu of options; (iv) all determinations with respect to any such future grants, including, but not limited to, the times when options shall be granted, the number of shares subject to each option, the option price, and the time or times when each option shall be exercisable, will be at the sole discretion of the Company; (v) the Participant's participation in the Plan is voluntary; (vi) the value of the Option is an extraordinary item of compensation which is outside the scope of the Participant's employment or consulting contract, if any; and (vii) the Option is not part of normal or expected compensation for purposes of calculating any severance, resignation, redundancy, end of service payments, bonuses, long-service awards, pension or retirement benefits or similar payments.

14. NOTICES.

Any notices required or permitted by the terms of this Agreement or the Plan shall be given by recognized courier service, facsimile, registered or certified mail, return receipt requested, addressed as follows:

If to the Company:

Spero Therapeutics, Inc.
675 Massachusetts Avenue
Cambridge, MA 0 2139
Attention: Chief Financial Officer

If to the Participant, at the address set forth on the Stock Option Grant Notice

or to such other address or addresses of which notice in the same manner has previously been given. Any such notice shall be deemed to have been given upon the earlier of receipt, one business day following delivery to a recognized courier service or three business days following mailing by registered or certified mail.

15. GOVERNING LAW.

This Agreement shall be governed by and construed in accordance with the laws of the State of Delaware, without giving effect to its internal principles governing the conflict of law. For the purpose of litigating any dispute that arises under this Agreement, the parties hereby consent to exclusive jurisdiction in the Commonwealth of

Massachusetts and agree that such litigation shall be conducted in the state courts of Suffolk County, Massachusetts or the federal courts of the United States for the District of Massachusetts.

16. BENEFIT OF AGREEMENT.

Subject to the provisions of the Plan and the other provisions hereof, this Agreement shall be for the benefit of and shall be binding upon the heirs, executors, administrators, successors and assigns of the parties hereto.

17. ENTIRE AGREEMENT.

This Agreement, together with the Plan, 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 (with the exception of acceleration of vesting provisions contained in any other agreement with the Company). No statement, representation, warranty, covenant or agreement 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. Notwithstanding the foregoing in all events, this Agreement shall be subject to and governed by the Plan.

18. MODIFICATIONS AND AMENDMENTS.

The terms and provisions of this Agreement may be modified or amended as provided in the Plan.

19. WAIVERS AND CONSENTS.

Except as provided in the Plan, the terms and provisions of this Agreement may be waived, or consent for the departure therefrom granted, only by 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.

20. DATA PRIVACY.

By entering into this Agreement, the Participant: (i) authorizes the Company and each Affiliate, and any agent of the Company or any Affiliate administering the Plan or providing Plan recordkeeping services, to disclose to the Company or any of its Affiliates such information and data as the Company or any such Affiliate shall request in order to facilitate the grant of options and the administration of the Plan; and (ii) authorizes the Company and each Affiliate to store and transmit such information in electronic form for the purposes set forth in this Agreement.

[REMAINDER OF PAGE INTENTIONALLY LEFT BLANK]

Exhibit A

NOTICE OF EXERCISE OF STOCK OPTION

[Form for Shares registered in the United States]

To: Spero Therapeutics, Inc.

IMPORTANT NOTICE: This form of Notice of Exercise may only be used at such time as the Company has filed a Registration Statement with the Securities and Exchange Commission under which the issuance of the Shares for which this exercise is being made is registered and such Registration Statement remains effective.

Ladies and Gentlemen:

I hereby exercise my Stock Option to purchase _____ shares (the "Shares") of the common stock, $0.001 par value, of Spero Therapeutics, Inc. (the "Company"), at the exercise price of $_____ per share, pursuant to and subject to the terms of that Stock Option Grant Notice dated _____, 20__.

I understand the nature of the investment I am making and the financial risks thereof. I am aware that it is my responsibility to have consulted with competent tax and legal advisors about the relevant national, state and local income tax and securities laws affecting the exercise of the Option and the purchase and subsequent sale of the Shares.

I am paying the option exercise price for the Shares as follows:

Please issue the Shares (check one):

☐ to me; or

☐ to me and _____, as joint tenants with right of survivorship,

at the following address:

My mailing address for stockholder communications, if different from the address listed above, is:

Very truly yours,

Participant (signature)

Print Name

Date

Exhibit 10.20
Confidential
[***]

LICENSE AGREEMENT

BETWEEN

NEW PHARMA LICENSE HOLDINGS LIMITED

AND

EVEREST MEDICINES II LIMITED

***Portions of the exhibit, indicated by the mark "[***],"* were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.**

Confidential ***Execution Version***

LICENSE AGREEMENT

This LICENSE AGREEMENT (this "**Agreement**") is made as of January 1, 2019 ("**Effective Date**"), by and among **New Pharma License Holdings Limited**, a company organized under the laws of Malta having registration number C 75891 ("**NPLH**") and its principal place of business at 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts, 02139, **Everest Medicines II Limited**, a company incorporated under the laws of the Cayman Islands ("**Everest**") having its registered office at Vistra (Cayman) Limited, P. O. Box 31119, Grand Pavilion, Hibiscus Way, 802 West Bay Road, Grand Cayman, KY1 – 1205, Cayman Islands, and, solely for purposes of Sections 2.3(d) and 2.12 (Option to SPR741), Spero Potentiator, Inc., a Delaware corporation ("**Potentiator**") having its principal place of business at 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts, 02139. Everest, NPLH and Potentiator are referred to individually as a "**Party**" and collectively as the "**Parties**."

RECITALS

WHEREAS, NPLH owns certain intellectual property relating to a compound known as SPR206 being investigated as an antibiotic against multi-drug resistant and extensively drug resistant bacterial strains;

WHEREAS, Potentiator owns certain intellectual property relating to a compound known as SPR741 being investigated as a potentiator of antibiotic activity;

WHEREAS, each of NPLH and Potentiator are direct or indirect wholly-owned subsidiaries of Spero Therapeutics, Inc., a Delaware corporation ("**Spero Parent**");

WHEREAS, NPLH wishes to grant a license to Everest, and Everest wishes to take a license, under such intellectual property rights of NPLH to develop and commercialize SPR206 in certain territories in accordance with the terms and conditions set forth below;

WHEREAS, Potentiator wishes to grant an exclusive option to Everest, and Everest wishes to have an exclusive option, to negotiate for an exclusive license to use such intellectual property rights of Potentiator to develop and commercialize SPR741 in certain territories in accordance with the terms and conditions set forth below; and

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants herein contained, the receipt and sufficiency which are hereby acknowledged, the Parties hereby agree as follows.

ARTICLE 1
DEFINITIONS

Unless the context otherwise requires, the terms in this Agreement with initial letters capitalized, shall have the meanings set forth below, or the meaning as designated in the indicated places throughout this Agreement.

1.1 "**Active Pharmaceutical Ingredient**" or "**API**" means any substance intended to be used in a pharmaceutical product that when used becomes an active ingredient of that product intended to exert a pharmacological, immunological or metabolic action with a view to restoring, correcting or modifying physiological functions in man or animal; but excluding formulation components such as coatings, stabilizers, excipients or solvents, adjuvants or controlled release technologies.

1.2 "**Affiliate**" means, with respect to a Party, any Person that, directly or indirectly through one or more intermediaries, controls, is controlled by, or is under common control with that Party, but for only so long as such control exists. For the purpose of this definition, "control" (including, with correlative meaning, the terms "controlled by" and "under common control") means (a) to possess, directly or indirectly, the power to direct the management or policies of an entity, whether through ownership of voting securities, by contract relating to voting rights or corporate governance, or otherwise; or (b) direct or indirect beneficial ownership of more than fifty percent (50%), or such lesser percentage which is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction, of the voting share capital or other equity interest in such entity.

1.3 "**Applicable Laws**" means the applicable provisions of any and all national, supranational, regional, federal, state and local laws, treaties, statutes, rules, regulations, administrative codes, guidance, ordinances, judgments, decrees, directives, injunctions, orders, permits (including MAAs) of or from any court, arbitrator, Regulatory Authority or Government Authority having jurisdiction over or related to the subject item, including the FFDCA, DAL, and the Provisions for Drug Registration of NMPA.

1.4 "**Auditor**" has the meaning set forth in Section 8.10 (Audit Dispute).

1.5 "**Business Day**" means a day other than a Saturday, Sunday or a bank or other public holiday in Mainland China, Hong Kong or The Commonwealth of Massachusetts in United States.

1.6 "**Calendar Quarter**" means each respective period of three (3) consecutive months ending on 31 March, 30 June, 30 September, and 31 December, except that the first Calendar Quarter of the Term shall commence on the Effective Date and end on the day immediately prior to the first 1 January, 1 April, 1 July or 1 October to occur after the Effective Date, and the last Calendar Quarter shall end on the last day of the Term.

1.7 "**Calendar Year**" means each successive period of 12 calendar months commencing on 1 January and ending on 31 December except that the first Calendar Year of the Term shall commence on the Effective Date and end on 31 December of the year in which the Effective Date occurs and the last Calendar Year of the Term shall commence on 1 January of the year in which the Term ends and end on the last day of the Term.

1.8 "**CFR**" means the U.S. Code of Federal Regulations.

1.9 "**Challenge**" means to contest or assist, directly or indirectly, in the contesting of the validity or enforceability of any of the NPLH Patents, in whole or in part, in any court,

arbitration proceeding or other tribunal, including the United States Patent and Trademark Office and the United States International Trade Commission. For the avoidance of doubt, the term "contest" includes: (a) filing an action under 28 U.S.C. §§ 2201-2202 seeking a declaration of invalidity or unenforceability of any NPLH Patents; (b) citation to the United States Patent and Trademark Office pursuant to 35 U.S.C. § 301 of prior art patents or printed publications or statements of the patent owner concerning the scope of any of the NPLH Patents; (c) filing a request under 35 U.S.C. § 302 for re-examination of any of the NPLH Patents; (d) filing, or joining in, a petition under 35 U.S.C. § 311 to institute inter partes review of any NPLH Patents or any portion thereof; (e) filing, or joining in, a petition under 35 U.S.C. § 321 to institute post-grant review of the NPLH Patents or any portion thereof; (f) provoking or becoming a party to an interference with an application for any of the NPLH Patents pursuant to 35 U.S.C. § 135; (g) filing or commencing any re-examination, opposition, cancellation, nullity or similar proceedings against any of the NPLH Patents in any country; or (h) any foreign equivalents of subsection (a) through (g) applicable in the Territory.

1.10 "**Claims**" means all Third Party demands, claims, actions, proceedings and liabilities (whether criminal or civil, in contract, tort or otherwise) for losses, damages, legal costs and other expenses of any nature.

1.11 "**Clinical Study Report**" means an "integrated" full report of an individual study of SPR206 that includes statistical descriptions, presentations and analyses, incorporating tables and figures into the main text of the report or at the end of the text, with appendices containing such information as the protocol, sample case report forms, investigator-related information, information related to the test drugs/investigational products including active control/comparators, technical statistical documentation, related publications, patient data listings, and technical statistical details such as derivations, computations, analyses, and computer output, prepared under the guidelines of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.

1.12 "**CMC**" means chemistry, manufacturing, and controls.

1.13 "**Combination Product**" means any Licensed Product comprised of the following, either formulated together (i.e., a fixed dose combination), packaged together and sold for a single price, or co-administered or jointly provided to patients (but which shall be limited to anti-infectious product only), whether or not packaged together: (a) the Compound, and (b) at least one other Active Pharmaceutical Ingredient.

1.14 **"Commercial Supply Agreement**" has the meaning set forth in Section 6.1(b) (Commercial Supply Agreement).

1.15 "**Commercialization**" means the conduct of all activities undertaken before and after Regulatory Approval has been obtained relating to the promotion, marketing, sale and distribution (including importing, exporting, transporting for commercial sales, customs clearance, warehousing, invoicing, handling and delivering the Licensed Products to customers) of the Compound or the Licensed Products, including: (a) sales force efforts, detailing, advertising, medical education, planning, marketing, sales force training, and sales and

distribution; and (b) scientific and medical affairs. For clarity, Commercialization does not include any Development activities, whether conducted before or after Regulatory Approval. "**Commercialize**" and "**Commercializing**" have correlative meanings.

1.16 "**Commercialization Plan"** has the meaning set forth in Section 7.2 (Commercialization Plan).

1.17 "**Commercially Reasonable Efforts**" means, with respect to each Party's obligations under this Agreement relating to the Development, Manufacturing, and Commercialization activities with respect to the Compound or the Licensed Products, the carrying out of such activities using efforts and resources that are consistent with the exercise of customary scientific and business practices as applied in the pharmaceutical industry for a company of a similar stage and size as the entity and having similar resources, for development, regulatory, manufacturing and commercialization activities conducted with respect to products at a similar stage of development or commercialization and having similar commercial potential, taking into account relative safety and efficacy, product profile, the regulatory environment, payers' policies and regulations, competitiveness of the marketplace and the market potential of such products, the nature and extent of market exclusivity, including patent coverage and regulatory data protection, and price and reimbursement status. The Parties hereby agree that the level of effort may be different for different markets and may change over time, reflecting changes in the status of the aforementioned attributes and potential of the Compound and the Licensed Products. When used regarding obligations under this Agreement other than the Development, Manufacturing, and Commercialization activities with respect to the Compound or the Licensed Products, the term "**Commercially Reasonable Efforts**" shall mean the carrying out of such activities using commercially reasonable efforts and financial, personnel and other resources that are consistent with the exercise of customary business practices as applied in the carrying out of such activities generally by and on behalf of biopharmaceutical companies of a similar stage and size and having similar resources.

1.18 "**Compound**" means SPR206.

1.19 "**Confidential Information**" of a Party means all Know-How, Inventions, unpublished patent applications and other information and data of a financial, commercial, business, operational or technical nature of such Party that is disclosed or made available by or on behalf of such Party or any of its Affiliates to the other Party or any of its Affiliates, whether made available orally, in writing or in electronic or other form. The terms of this Agreement are the Confidential Information of both Parties.

1.20 "**Control**" or "**Controlled**" means, with respect to any Know-How, Patents, Regulatory Documentation or other intellectual property rights, that a Party has the legal authority or right (whether by ownership, license or otherwise, other than by virtue of any license granted to such Party by the other Party pursuant to this Agreement) to grant a license, sublicense, access or other right (as applicable) under such Know-How, Patents, Regulatory Documentation or other intellectual property rights to the other Party on the terms and conditions set forth herein, in each case without breaching the terms of any agreement with a Third Party, infringing third party intellectual property, or misappropriating third party trade secrets.

1.21 "**Controlling Party**" has the meaning set forth in Section 9.6 (Invalidity or Unenforceability Defenses or Actions)

1.22 **"Corporate Names"** has the meaning set forth in Section 1.125 (Spero Trademarks).

1.23 "**Cost of Goods**" means, with respect to any Compound or any Licensed Product, the fully absorbed cost to manufacture such Compound or Licensed Product in finished form for Development and/or Commercialization use, which means: (a) in the case of products, intermediates, API and services acquired from one or more Third Parties, all documented payments made to such Third Parties or direct material costs directly related to such products, intermediates, API and services, including without limitation, all costs incurred in purchasing materials, sales, excise and other taxes imposed thereon, customs duties, import, export and other charges levied by Governmental Authorities, all costs of packaging, shipping and insuring such materials; and (b) in the case of manufacturing services performed by a Party or its Affiliates, including manufacturing services that are reasonably necessary to support products and services acquired from Third Parties as contemplated in subsection (a), the actual unit costs of manufacture, with no markup of any nature. The remainder of this definition is only applicable for determining costs of manufacturing services performed by a Party or its Affiliates as contemplated by subsection (b). Actual unit costs shall consist of direct material costs, direct labor costs, and manufacturing overhead directly attributable to such Compound or Licensed Product, all calculated in accordance with GAAP, but without allocation of idle capacity, all to the extent provided, procured or incurred in connection with the manufacture of such Compound or Licensed Product. Direct material costs shall include the costs incurred in purchasing materials, including sales, excise and other taxes imposed thereon, customs duties, import, export and other charges levied by Governmental Authorities, and all costs of packaging, shipping and insuring such components. Direct labor costs shall include the cost of: (i) employees working in direct manufacturing and packaging of such Compound or Licensed Product; and (ii) direct quality control and quality assurance activities. Manufacturing overhead attributable to such Compound or Licensed Product shall include a reasonable allocation of indirect labor costs (not previously included in direct labor costs). Manufacturing overhead shall in no event exceed [***]% of the sum of the direct material costs and direct labor costs. Cost of Goods under the preceding subsection (b) specifically excludes profit margins of NPLH or its Affiliates.

1.24 **"CTA"** means a Clinical Trial Application that is required to initiate a clinical trial for registering a drug product under the Drug Administration Law of the People's Republic of China and the Provisions for Drug Registration of NMPA, and equivalents thereof under future Chinese laws and regulations, and the laws and regulations of other countries and jurisdictions in the Territory, in each as the same may be amended from time to time.

1.25 "**DAL**" means the Drug Administration Law of the People's Republic of China and the equivalent laws of other countries and jurisdictions in the Territory, in each as the same may be amended from time to time.

1.26 "**Develop**" or "**Development**" means to develop (including clinical, non-clinical and CMC development), analyze, test and conduct preclinical, clinical and all other regulatory

trials for the Compound or Licensed Product, including all post-approval clinical trials, as well as all related regulatory activities and any and all activities pertaining to new Indications, pharmacokinetic studies and all related activities including work on new formulations, new methods of treatment and CMC activities including new manufacturing methods. "**Developing**" and "**Development**" have correlative meanings.

1.27 "**Development Plan"** has the meaning set forth in Section 4.2 (Development Plan).

1.28 "**Diligence Meeting**" has the meaning set forth in Section 4.3(b) (Specific Diligence Events).

1.29 "**Diligence Meeting Date**" has the meaning set forth in Section 4.3(b) (Specific Diligence Events)

1.30 "**Diligence Milestone**" has the meaning set forth in Section 4.3(b) (Specific Diligence Events).

1.31 "**Diligence Target Dates**" has the meaning set forth in Section 4.3(b) (Specific Diligence Events).

1.32 "**Disclosing Party"** has the meaning set forth in Section 10.1(a) (Duty of Confidence - subsection (a)).

1.33 "**Dispute"** has the meaning set forth in Section 14.10(a) (Dispute Resolution - subsection (a)).

1.34 "**Dollar**" means U.S. dollars, and "$" shall be interpreted accordingly.

1.35 "[***] **Study**" means a clinical study to measure [***].

1.36 "**Everest Development Data**" means any (a) pharmacology, toxicology and other biological data Co ntrolled by Everest related to the Compound or any Licensed Product or otherwise included in, or filed in support of, the Regulatory Documentation filed by Everest in the Territory and (b) clinical data Controlled by Everest related to the Compound or any Licensed Product or otherwise included in, or filed in support of, the Regulatory Documentation filed by Everest in the Territory.

1.37 "**Everest Know-How**" means all Know-How that Everest Controls as of the Effective Date or during the Term that is necessary or reasonably useful for the Development, Manufacture, Commercialization or other Exploitation of any Compound or Licensed Product in the Licensed Field, including Everest Sole Inventions, Everest's interest in any Joint Inventions, Everest Development Data and Everest's Regulatory Documentation.

1.38 "**Everest Indemnitees**" has the meaning set forth in Section 13.1 (Indemnification by Spero).

1.39 "**Everest Patents**" means all Patents that Everest Controls as of the Effective Date or during the Term that are necessary or reasonably useful for the Development, Manufacture, Commercialization or other Exploitation of any Compound or any Licensed Product in the Licensed Field, including any Everest Sole Invention Patents and Everest's interest in the Joint Patents in the Territory.

1.40 "**Everest Sole Inventions**" means any Inventions that are conceived and reduced to practice solely by employees of, or consultants or service providers to, Everest, at any time during the Term of this Agreement and that are made, generated, conceived or otherwise invented as a result of a Party exercising its rights or carrying out its obligations under this Agreement, whether directly or via its Affiliates, agents or independent contractors.

1.41 "**Everest Sole Invention Patents**" means any Patents that contain one or more claims that cover Everest Sole Inventions.

1.42 "**Everest Technology**" means the Everest Patents and the Everest Know-How.

1.43 "**Excluded Claim"** has the meaning set forth in Section 14.10(g) (Dispute Resolution - subsection (g)).

1.44 **"Executive Officers"** has the meaning set forth in Section 3.3(b) (JDC Decision Making - subsection (a)).

1.45 "**Exploit**" means to make, have made, import, use, sell or offer for sale, including to research, Develop, Commercialize, register, Manufacture, have Manufactured, hold or keep (whether for disposal or otherwise), have used, export, transport, distribute, promote, market or have sold or otherwise dispose of.

1.46 "**Exploitation**" means the act of Exploiting the Compound, product or process.

1.47 "**FDA**" means the United States Food and Drug Administration or any successor entity thereto.

1.48 "**FFDCA**" means the United States Federal Food, Drug, and Cosmetic Act, as amended from time to time, together with any rules, regulations and requirements promulgated thereunder (including all additions, supplements, extensions and modifications thereto).

1.49 "**First Commercial Sale**" means, with respect to any Licensed Product in any jurisdiction in the Territory, the first arm's length sale of such Licensed Product by Everest, its Affiliates or Sublicensees to a Third Party for monetary value for use or consumption of such Licensed Product by the end user in the general public after Regulatory Approval for such Licensed Product in such jurisdiction has been granted. Sales prior to receipt of Regulatory Approval for such Licensed Product, such as so-called "treatment IND sales," "named patient sales," and "compassionate use sales," shall not be construed as a First Commercial Sale.

1.50 "**First Diligence Notice**" has the meaning set forth in Section 4.3(b) (Specific Diligence Events).

1.51 "**Fiscal Year**" means the period from January 1 of a Calendar Year through December 31 of such Calendar Year.

1.52 "**GAAP**" means the then-current Generally Accepted Accounting Principles or International Financial Reporting Standards (IFRS), whichever is adopted as the standard financial accounting guideline in the United States for public companies, as consistently applied.

1.53 "**Generic Competition**" means, on a Licensed Product-by-Licensed Product and jurisdiction-by-jurisdiction basis, that, in a given Calendar Quarter, one or more Third Parties is selling one or more Generic Products in such jurisdiction and the unit volume of all Generic Products to such Licensed Product sold in such jurisdiction in such Calendar Quarter is equal to or greater than [***] percent ([***]%) of the combined unit volume of such Generic Products and such Licensed Product sold in such jurisdiction in such Calendar Quarter, where the number of units of the Generic Products and the Licensed Product sold in the relevant jurisdiction and Calendar Quarter are as reported by IQVIA or any successor thereto (or based on equivalent data reported by any other independent sales auditing firm mutually agreed by the Parties if IQVIA data are not available).

1.54 "**Generic Product**" means, with respect to a Licensed Product, any product that contains the same Compound as such Licensed Product and that is sold under an approved Marketing Authorization Application granted by a Regulatory Authority to a Third Party that is not a Sublicensee of Everest or its Affiliates and did not obtain such product in a chain of distribution that includes any of Everest, its Affiliates, or its Sublicensees.

1.55 **"Good Manufacturing Practices"** or **"GMP"** shall mean all applicable Good Manufacturing Practices standards, including, as applicable, those standards required by any Regulatory Authority in the Territory.

1.56 "**Government Authority**" means any federal, state, national, state, provincial or local government, or political subdivision thereof, or any multinational organization or any authority, agency or commission entitled to exercise any administrative, executive, judicial, legislative, police, regulatory or taxing authority or power, any court or tribunal (or any department, bureau or division thereof, or any governmental arbitrator or arbitral body).

1.57 "**Hong Kong**" means the Hong Kong Special Administrative Region of the People's Republic of China.

1.58 "**IND**" means a CTA or any other investigational new drug application, clinical trial application, clinical trial exemption or similar or equivalent application or submission for approval to conduct human clinical investigation filed with or submitted to the NMPA in conformance with the requirements of the NMPA, or any other Regulatory Authority of any jurisdiction in the Territory in conformance with the requirements of such Regulatory Authority.

1.59 "**Indemnification Claim Notice**" has the meaning set forth in Section 13.3(a) (Notice of Claim).

1.60 "**Indemnified Party**" has the meaning set forth in Section 13.3(a) (Notice of Claim).

1.61 "**Indemnifying Party**" has the meaning set forth in Section 13.3(a) (Notice of Claim).

1.62 "**Indication**" means a separate and distinct disease, disorder, illness or health condition for which a separate MAA approval is required.

1.63 "**Indirect Costs**" means, with respect to a multi-regional clinical trial, all Third Party costs and expenses incurred by NPLH or Everest to conduct such multi-regional clinical trial that are not directly allocable to a Party's territory (or to clinical sites within a Party's territory), including, without limitation, fees, costs and expenses for data management, clinical evaluation committees, data safety monitoring boards, physician consulting, investigator meetings, travel, document translation and other technology solutions and services that are not specific to a territory or a clinical site within a territory.

1.64 **"Infringed IP"** means, with respect to any jurisdiction in the Territory, (a) a claim of an issued and unexpired Patent (as may be extended through supplementary protection certificate or patent term extension or the like) that has not been cancelled, revoked, held invalid or unenforceable by a decision of a patent office or other Government Authority of competent jurisdiction from which no appeal can be taken (or from which no appeal was taken within the allowable time period) and which claim has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer or otherwise; (b) a claim of a Patent application pending for no more than [***] years that has not been cancelled, withdrawn or abandoned or finally rejected by an administrative agency action from which no appeal can be taken; or (c) any Know-How not in the public domain; in each of case (a) and (b) which such claim the JDC reasonably determines to be infringed by (i) Everest's Manufacturing, selling or offering for sale of the Compound or a Licensed Product and/or (ii) NPLH's Manufacturing, selling or offering for sale of the Compound or a Licensed Product; and in the case of (c), which Know-How the JDC reasonably determines to be necessary to (i) Everest's Manufacturing, selling or offering for sale of the Compound or a Licensed Product and/or (ii) NPLH's Manufacturing, selling or offering for sale of the Compound or a Licensed Product.

1.65 "**Initial Development Plan**" has the meaning set forth in Section 4.2 (Development Plan).

1.66 "**Initiation**" means, with respect to a clinical trial, the first dosing (whether with investigational drug, comparator drug or placebo) of the first subject in such clinical trial.

1.67 "**Initial Supply Agreement**" has the meaning set forth in Section 6.1 (Supply Agreement).

1.68 "**Initial Term**" has the meaning set forth in Section 11.1 (Term).

1.69 "**In-License Agreement**" has the meaning set forth in Section 2.4(b) (In-License Agreements).

1.70 "**Invention**" means any technical, scientific and other know-how and information, trade secrets, knowledge, technology, means, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences, ideas, technical assistance, designs, drawings, assembly procedures, computer programs, apparatuses, specifications, data, results and other material, including: biological, chemical, pharmacological, toxicological, pharmaceutical, physical and analytical, pre-clinical, clinical, safety, manufacturing and quality control data and information, including study designs and protocols, assays and biological methodology process, composition of matter, article of manufacture, discovery or finding, patentable or otherwise, that is made, generated, conceived or otherwise invented as a result of a Party exercising its rights or carrying out its obligations under this Agreement, whether directly or via its Affiliates, agents or independent contractors, including all rights, title and interest in and to the intellectual property rights therein. For clarity, "Invention" does not include NPLH Development Data or Everest Development Data.

1.71 "**Joint Development Committee**" or "**JDC**" has the meaning set forth in Section 3.1 (Joint Development Committee).

1.72 "**Joint Inventions**" means any Inventions that are conceived and reduced to practice jointly by employees of, or consultants or service providers to, NPLH and Everest, at any time during the Term of this Agreement and that are made, generated, conceived or otherwise invented as a result of NPLH and Everest exercising their rights or carrying out their obligations under this Agreement, whether directly or via their Affiliates, agents or independent contractors.

1.73 "**Joint Patents**" means any Patents that contain one or more claims that cover Joint Inventions.

1.74 "**Know-How**" means any information, including discoveries, improvements, modifications, processes, methods, techniques, protocols, formulas, data, inventions, know-how, trade secrets and results, patentable or otherwise, including physical, chemical, biological, toxicological, pharmacological, safety, and pre-clinical and clinical data, dosage regimens, control assays, and product specifications, but excluding any Patents.

1.75 "**Licensed Field**" means all therapeutic uses in humans.

1.76 "**Licensed Know-How**" means all Know-How that NPLH Controls as of the Effective Date or during the Term that is necessary or reasonably useful for the Development, Manufacture, Commercialization or other Exploitation of the Compound or any Licensed Product for use in the Licensed Field in the Territory, including all NPLH Sole Inventions, NPLH's interest in any NPLH Joint Inventions in the Territory, NPLH Development Data and NPLH's Regulatory Documentation (with respect to Compound or a Licensed Product).

1.77 "**Licensed Manufacturing Know-How**" has the meaning set forth in Section 6.2 (Manufacturing Technology Transfer).

1.78 "**Licensed Patents**" means all Patents Controlled by NPLH as of the Effective Date or during the Term that are necessary or reasonably useful for the Development,

Manufacture, Commercialization, or other Exploitation of the Compound or any Licensed Product for use in the Licensed Field in the Territory, including any NPLH Sole Invention Patents and NPLH's interest in the NPLH Joint Patents in the Territory. The NPLH Patents existing as of the Effective Date are listed on Exhibit A.

1.79 "**Licensed Product**" means any pharmaceutical product that contains the Compound, alone or in combination with one or more other molecules or agents in any dosage form or formulation. For purposes of this Agreement, with respect to a Licensed Product that has been approved for an initial Indication, the approval of such License Product for one or more additional Indications shall not constitute a new and separate Licensed Product.

1.80 "**Licensed Product Agreement**" means, with respect to the Compound or any Licensed Product, any agreement entered into by and between Everest or any of its Affiliates or its or their Sublicensees, on the one hand, and one or more Third Parties, on the other hand, that is necessary or reasonably useful for the Exploitation of the Compound or a Licensed Product in the Licensed Field in the Territory, including without limitation: (a) any agreement (other than this Agreement) pursuant to which Everest, any of its Affiliates or any of its or their Sublicensees receives any license or other rights to Exploit the Compound or a Licensed Product; (b) any supply agreement (other than the Initial Supply Agreement and the Commercial Supply Agreement) pursuant to which Everest, any of its Affiliates or any of its or their Sublicensees obtains quantities of the Compound or a Licensed Product; (c) any clinical trial agreements; (d) any contract research organization agreements; and (e) any service agreements.

1.81 "**Licensed Technology**" means the Licensed Patents and the Licensed Know-How.

1.82 "**MAA**" or "**Marketing Authorization Application**" means an application to the appropriate Regulatory Authority for approval to market a Licensed Product (but excluding Pricing Approval) in any particular jurisdiction, and all amendments, renewals and supplements thereto, including an NDA filed with the FDA in the U.S. or an NDA (or any future equivalent thereto as defined in the DAL and the Provisions for Drug Registration) filed with the NMPA in the Territory.

1.83 "**Mainland China**" means the People's Republic of China, including Hainan Island, but excluding Hong Kong, the Macau Special Administrative Region of the People's Republic of China and Taiwan.

1.84 "**Manufacture**" and "**Manufacturing**" means all activities related to the production, manufacture, processing, filling, finishing, packaging, labeling, in-process and finished testing, shipping, storing, or release of a product or any ingredient or intermediate thereof, including process development, process qualification and validation, scale-up, pre-clinical, clinical and commercial manufacture and analytic development, product characterization, test method development and stability testing, formulation, quality assurance and quality control of the any compound, product or intermediate, and regulatory affairs with respect to the foregoing.

1.85 "**Manufacturing Transfer Period**" has the meaning set forth in Section 6.2 (Manufacturing Technology Transfer).

1.86 "**Milestone Event**" has the meaning set forth in Section 8.2(a) - (8.2 Development and Regulatory Milestone Payments – clause (a)).

1.87 "**Milestone Payment**" has the meaning set forth in Section 8.2(a) - (8.2 Development and Regulatory Milestone Payments – clause (a)).

1.88 "**NDA**" means a New Drug Application (as more fully defined in 21 C.F.R. §314.5 et seq. or successor regulation) and all amendments and supplements thereto filed with the FDA and any other equivalent filings in the Territory.

1.89 "**Net Sales**" means, with respect to any Licensed Product, the gross amounts invoiced for sales or other dispositions of such Licensed Product (excluding transfer or dispositions of product at or below manufacturing cost, or without charge, for nonclinical or clinical purposes, research, commercial samples, compassionate use, indigent programs and humanitarian and charitable donations) by or on behalf of Everest, its Affiliates and Sublicensees to Third Parties, less the following deductions to the extent included in the gross invoiced sales price for such Licensed Product or otherwise paid or incurred by Everest or its Affiliates, as applicable, with respect to the sale or other disposition of such Licensed Product:

(a) normal and customary trade and quantity and cash discounts, allowances, and credits actually allowed and properly taken with respect to sales of such Licensed Product;

(b) credits or allowances given or made for rejection or return of previously sold Licensed Products or for retroactive price reductions and billing errors;

(c) discounts, rebates, reimbursements, and chargeback payments granted to managed health care organizations or other health care institutions (including hospitals), health care administrators, patient assistance or similar programs, pharmacy benefit managers (or equivalents thereof), wholesalers and other distributors, pharmacies and other retailers, group purchasing organizations or other buying groups, health maintenance organizations, national, state/provincial, local, and other governments, their agencies and purchasers and reimbursers, any other providers of health insurance coverage, or to trade customers;

(d) costs of freight, postage, insurance, and other transportation charges related to the distribution of such Licensed Product;

(e) any Taxes levied on or with respect to such Licensed Product or measured by the billing amount of such Licensed Product (excluding Taxes imposed on or with respect to net income, however, denominated);

(f) the portion of administrative fees paid during the relevant time period to group purchasing organizations or pharmaceutical benefit managers relating to such Licensed Product; and

(g) amounts invoiced for sales of Licensed Product that are written off as uncollectible after reasonable collection efforts, in accordance with GAAP and standard practices of the applicable party.

Such amounts shall be determined in accordance with GAAP, consistently applied. Any of the deductions listed above that involves a payment by Everest, its Affiliates or its or their Sublicensees shall be taken as a deduction in the Calendar Quarter in which the payment is accrued by such entity. For purposes of determining Net Sales, a Licensed Product shall be deemed to be sold when invoiced. Everest's, its Affiliates' or its or their Sublicensees' transfer of any Licensed Product to an Affiliate or Sublicensee shall not result in any Net Sales unless such Licensed Product is consumed or administered by such Affiliate or Sublicensee in the course of its commercial activities. With respect to any Licensed Product that is consumed or administered by Everest or its Affiliates or its or their Sublicensees, Net Sales shall include any amount billed or invoiced with respect to such consumption or administration, including any services provided directly in connection therewith.

In the event that a Licensed Product is sold as part of a Combination Product, then Net Sales for such product shall be determined by multiplying the net sales of the Combination Product (as calculated in accordance with analogous criteria as set forth above for the "Net Sales" definition) by the fraction, A / (A+B) where A is the weighted average sale price of such Licensed Product when sold separately in finished form, and B is the weighted average sale price of the other active compound or ingredient in the Combination Product sold separately in finished form.

In the event that the weighted average sale price of a Licensed Product can be determined but the weighted average sale price of the other active compound or ingredient in the Combination Product cannot be determined, then Net Sales for such product shall be calculated by multiplying the net sales of the Combination Product (as calculated in accordance with analogous criteria as set forth above for the "Net Sales" definition) by the fraction A / C where A is the weighted average sale price of such Licensed Product when sold separately in finished form and C is the weighted average sale price of the Combination Product.

In the event that the weighted average sale price of the other active compounds or ingredients in the Combination Product can be determined but the weighted average sale price of such Licensed Product cannot be determined, Net Sales for such product shall be calculated by multiplying the net sales of the Combination Product (as calculated in accordance with analogous criteria as set forth above for the "Net Sales" definition) by the following formula: one (1) minus B / C where B is the weighted average sale price of the other active compound or ingredient in the Combination Product when sold separately in finished form and C is the weighted average sale price of the Combination Product.

In the event that the weighted average sale price of both a Licensed Product and the other active compound or ingredient in the Combination Product cannot be determined, then Net Sales for such product shall be equal to [***] percent ([***]%) of the net sales of the Combination Product (as calculated in accordance with analogous criteria as set forth above for the "Net Sales" definition).

1.90 "**NMPA**" means the National Medical Products Administration of the People's Republic of China, f.k.a. China Food and Drug Administration, or its successor.

1.91 "**NPLH CMO**" has the meaning set forth in Section 6.2 (Manufacturing Technology Transfer)

1.92 "**NPLH Development Data**" means any (a) pharmacology, toxicology and other biological data Controlled by NPLH related to the Compound or any Licensed Product or otherwise included in, or filed in support of, the Regulatory Documentation filed by NPLH outside of the Territory and (b) clinical data Controlled by NPLH related to the Compound or any Licensed Product or otherwise included in, or filed in support of, the Regulatory Documentation filed by NPLH outside of the Territory

1.93 "**NPLH Indemnitees**" has the meaning set forth in Section 13.2 (Indemnification by Everest).

1.94 "**NPLH Sole Inventions**" means any Inventions that are conceived and reduced to practice solely by employees of, or consultants or service providers to, NPLH, at any time during the Term of this Agreement and that are made, generated, conceived or otherwise invented as a result of a Party exercising its rights or carrying out its obligations under this Agreement, whether directly or via its Affiliates, agents or independent contractors.

1.95 "**NPLH Sole Invention Patents**" means any Patents that contain one or more claims that cover NPLH Sole Inventions.

1.96 "**Option Notice**" has the meaning set forth in Section 2.3(d).

1.97 "**Option Fee**" has the meaning set forth in Section 2.12(a).

1.98 "**Option Period**" has the meaning set forth in Section 2.3(d).

1.99 "**Patent**" means all patents and patent applications, including all provisionals, divisionals, reissues, reexaminations, renewals, continuations, continuations-in-part, substitute applications, priority applications and inventors' certificates, extensions and supplemental certificates and any and all foreign equivalents of the foregoing.

1.100 "**Payment**" has the meaning set forth in Section 8.8(b).

1.101 "**Permitted Liens**" means: (a) liens securing indebtedness for borrowed money; (b) security interests in assets to secure indebtedness for borrowed money; (c) purchase money liens on secured purchase money indebtedness; (d) liens to secure capitalized lease obligations; (e) liens for Taxes, the nonpayment of which is being contested in good faith by appropriate proceedings and for which adequate reserves or appropriate provisions, if any, as shall be required by GAAP shall have been set aside on such Person's books; (f) statutory or similar liens of carriers, warehousemen, mechanics, laborers, materialmen and landlords incurred in the ordinary course of business for sums not yet due or being contested in good faith; (g) liens arising out of judgments or awards, and appeals and similar bonds incident to the conduct of

legal actions against such Person, which such Person shall then be prosecuting an appeal or other proceedings for review; and (h) liens (including deposits) incurred in the ordinary course of business to secure bids or tenders or the performance of statutory obligations, leases, contracts, surety and appeal bonds, performance bonds, and other obligations of a like nature, and other encumbrances incidental to the normal conduct of the business of such Person.

"**Person**" means any individual, partnership, limited liability company, firm, corporation, association, trust, unincorporated organization or other entity.

1.103 "**Phase 1 Clinical Trial**" means a human clinical trial that would satisfy the requirements for a Phase 1 study as defined in 21 CFR § 312.21(a) (or any amended or successor regulations) or any equivalent regulations in jurisdictions in the Territory, regardless of where such clinical trial is conducted.

1.104 "**Phase 3 Clinical Trial**" means a human clinical trial that would satisfy the requirements for a Phase 3 study as defined in 21 CFR § 312.21(c) (or any amended or successor regulations) or any equivalent regulations in jurisdictions in the Territory, regardless of where such clinical trial is conducted.

1.105 "**Polymyxin Class Compound**" has the meaning set forth in Section 2.8 (Non-Compete).

1.106 "**Potentiator**" has the meaning set forth in the introduction to this Agreement.

1.107 "**Pricing Approval**" means such governmental approval, agreement, determination or decision establishing prices for a Licensed Product that can be charged and/or reimbursed in a regulatory jurisdiction where the applicable Government Authority approves or determines the price and/or reimbursement of pharmaceutical products and where such approval or determination is necessary for the commercial sale of such Licensed Product in such jurisdiction.

1.108 "**Product Infringement**" has the meaning set forth in Section 9.4(a) (Notice).

1.109 "**Product Trademarks**" means the Trademark(s) used or to be used by Everest or its Affiliates or its or their Sublicensees for the Commercialization of Licensed Products in the Licensed Field in the Territory and any registrations thereof or any pending applications relating thereto in the Territory (excluding, in any event, any Corporate Names and any Spero Trademarks that consist of or include any corporate name or corporate logo of Spero Parent, NPLH or its or their Affiliates or its or their (sub)licensees (or Sublicensees)).

1.110 "**Receiving Party"** has the meaning set forth in Section 10.1(a) (Duty of Confidence - subsection (a)).

1.111 "**Reimbursement Rate**" means, with respect the costs to NPLH or Everest of conducting a clinical trial, the costs of services provided by one Party to the other Party on an FTE-based compensation rate or any similar FTE-based costs to be paid for or reimbursed hereunder, a blended FTE rate of $[***] per annum, or $[***] per hour.

1.112 "**Regulatory Approval**" means, with respect to a jurisdiction in the Territory, any and all approvals (including approvals of Marketing Authorization Applications), licenses, registrations or authorizations of any Regulatory Authority necessary to commercially distribute, sell or market a Licensed Product in such jurisdiction, including, where applicable: (a) pricing or reimbursement approval in such jurisdiction; (b) pre- and post-approval marketing authorizations (including any prerequisite Manufacturing approval or authorization related thereto); and (c) labelling approval.

1.113 "**Regulatory Authority**" means any applicable Government Authority responsible for granting Regulatory Approvals for any Licensed Product, including the FDA, the NMPA, and any corresponding national or regional regulatory authorities.

1.114 **"Regulatory Documentation"** means: all (a) applications (including all Regulatory Filings, INDs, CTAs and Marketing Authorization Applications), registrations, licenses, authorizations and approvals (including Regulatory Approvals); (b) correspondence and reports submitted to or received from Regulatory Authorities (including minutes and official contact reports relating to any communications with any Regulatory Authority) and all supporting documents with respect thereto, including all adverse event files and complaint files; and (c) clinical and other data contained or relied upon in any of the foregoing; in each case (a), (b) and (c)) relating to the Compound or a Licensed Product.

1.115 "**Regulatory Exclusivity**" means any exclusive marketing rights or data exclusivity rights conferred by any Regulatory Authority with respect to a pharmaceutical product other than Patents, and including, without limitation, orphan drug exclusivity, new chemical entity exclusivity, data exclusivity or pediatric exclusivity.

1.116 "**Regulatory Filings**" means, with respect to the Compound or Licensed Products, any submission to a Regulatory Authority of any appropriate regulatory application specific to the Compound or Licensed Products, and shall include, without limitation, any submission to a regulatory advisory board and any supplement or amendment thereto. For the avoidance of doubt, Regulatory Filings shall include any IND, CTA, NDA, MAA, Regulatory Approval or the corresponding application in any other country or jurisdiction.

1.117 "**Representative**" has the meaning set forth in Section 10.1(c) (Duty of Confidence - Subsection (c)).

1.118 "**Respective Territory**" means, in the case of Everest, the Territory, and in the case of NPLH, all countries of the world outside the Territory.

1.119 "**Retained Rights**" means, with respect to the Compound and Licensed Products, the rights of NPLH, its Affiliates and its and their licensors, (sub)licensees and contractors to:

(a) perform its and their obligations under this Agreement;

(b) Manufacture, have Manufactured, Develop and have Developed the Compound or Licensed Products, within the Territory solely for Exploitation outside the Territory; and

(c) Develop, Manufacture, Commercialize and otherwise Exploit the Compound and Licensed Products for any and all purposes outside the Territory.

1.120 "**Royalty Term**" has the meaning set forth in Section 8.4(b) (Royalty Term).

1.121 "**SEC**" has the meaning set forth in Section 10.5 (Publicity/Use of Names - subsection (a)).

1.122 "**Senior Officer**" means, with respect to NPLH, the Chief Executive Officer of Spero Parent, and with respect to Everest, its Chief Executive Officer.

1.123 "[***]" has the meaning set forth in Section 14.10(b) (Dispute Resolution).

1.124 "**Spero Parent**" has the meaning set forth in the recitals to this Agreement.

1.125 "**Spero Trademarks**" means any corporate name or corporate logo of Spero Parent, NPLH or its or their Affiliates, and any Trademark that consists of or includes any corporate name or corporate logo of Spero Parent, NPLH or its or their Affiliates ("**Corporate Names**"), including the Spero Trademarks, names and logos identified on Exhibit B hereto and such other Trademarks, names and logos as NPLH may designate in a writing sent to Everest from time to time during the Term.

1.126 "**SPR206**" means the compound known as SPR206 and having the chemical structure shown in Exhibit C and [***].

1.127 "**SPR741**" means the compound known as SPR741 and having the chemical structure shown in Exhibit D and [***].

1.128 "**Sublicense**" means a license or sublicense granted by Everest (or a Sublicensee) to Develop, make, use, import, promote, offer for sale or sell the Compound or any Licensed Product, including any license given to any of the rights granted to Everest under Section 2.1(Licenses to Everest).

1.129 "**Subcontractor**" has the meaning set forth in Section 2.9 (Subcontracting).

1.130 "**Sublicensee**" means a Third Party to whom Everest or its Affiliate has granted a Sublicense in accordance with the terms of this Agreement.

1.131 "**Successive Term**" has the meaning set forth in Section 11.1 (Term).

1.132 "**Tax**" or "**Taxes**" means any (a) all federal, provincial, territorial, state, municipal, local, foreign or other taxes, imposts, rates, levies, assessments and other charges in the nature of a tax (and all interest and penalties thereon and additions thereto imposed by any Government Authority), including without limitation all income, excise, franchise, gains, capital, real property, goods and services, transfer, value added, gross receipts, windfall profits, severance, ad valorem, personal property, production, sales, use, license, stamp, documentary stamp, mortgage recording, employment, payroll, social security, unemployment, disability,

escheat, estimated or withholding taxes, and all customs and import duties, together with all interest, penalties and additions thereto imposed with respect to such amounts, in each case whether disputed or not; (b) any liability for the payment of any amounts of the type described in subsection (a) as a result of being or having been a member of an affiliated, consolidated, combined or unitary group; and (c) any liability for the payment of any amounts as a result of being party to any tax sharing agreement or arrangement or as a result of any express or implied obligation to indemnify any other person with respect to the payment of any amounts of the type described in subsection (a) or (b).

1.133 "**Term**" has the meaning set forth in Section 11.1 (Term).

1.134 "**Territory**" means Greater China (Mainland China, Hong Kong, the Macau Special Administrative Region of the People's Republic of China, and Taiwan), the Republic of Korea (South Korea) and Southeast Asia (the Republic of Singapore, Malaysian Federation, Kingdom of Thailand, the Republic of Indonesia, Socialist Republic of Vietnam and the Republic of the Philippines).

1.135 "**Third Party**" means any Person other than a Party or an Affiliate of a Party.

1.136 "**Third Party Infringement Claim**" has the meaning set forth in Section 9.5 (Infringement claims by Third Parties).

1.137 "**Trademark**" means any word, name, symbol, color, shape, designation or any combination thereof, including any trademark, service mark, trade name, brand name, sub-brand name, trade dress, product configuration rights, program name, delivery form name, certification mark, collective mark, logo, tagline, slogan, design or business symbol, that functions as an identifier of source, origin or quality, whether or not registered, and all statutory and common law rights therein and all registrations and applications therefor, together with all goodwill associated with, or symbolized by, any of the foregoing.

1.138 "**Transfer Tax**" has the meaning set forth in Section 8.8(c) (Transfer Tax).

1.139 "**United States**" or "**U.S.**" means the United States of America including its territories and possessions.

1.140 "**Valid Claim**" means, with respect to any jurisdiction in the Territory, (a) a claim of an issued and unexpired Patent (as may be extended through supplementary protection certificate or patent term extension or the like) that has not been cancelled, revoked, held invalid or unenforceable by a decision of a patent office or other Government Authority of competent jurisdiction from which no appeal can be taken (or from which no appeal was taken within the allowable time period) and which claim has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer or otherwise; or (b) a claim of a Patent application pending for no more than [***] years that has not been cancelled, withdrawn or abandoned or finally rejected by an administrative agency action from which no appeal can be taken; provided that in each of (a) and (b) in any jurisdiction in the Territory, a Valid Claim shall cease to be a Valid Claim in such jurisdiction if it does not block or prevent the entry, or Commercialization, of Generic Products.

1.141 Interpretation. In this Agreement, unless otherwise specified:

(a) "includes" and "including" shall mean, respectively, includes without limitation and including without limitation;

(b) words denoting the singular shall include the plural and vice versa and words denoting any gender shall include all genders;

(c) words such as "herein", "hereof", and "hereunder" refer to this Agreement as a whole and not merely to the particular provision in which such words appear; and

(d) the Exhibits and other attachments form part of the operative provision of this Agreement and references to this Agreement shall include references to the Exhibits and attachments.

ARTICLE 2
LICENSES

2.1 License to Everest.

(a) Subject to the terms and conditions of this Agreement, NPLH hereby grants to Everest an exclusive (even as to NPLH), royalty-bearing license under the NPLH Licensed Technology solely to Exploit Licensed Products in the Licensed Field in the Territory, with the right to grant sublicenses in accordance with Section 2.3 (Sublicense Rights).

(b) The United States federal government retains rights in certain of the Licensed Patents pursuant to 35 U.S.C. §§ 200-212 and 37 C.F.R. § 401 et seq., and any right granted in this Agreement greater than that permitted under 35 U.S.C. §§ 200-212 or 37 C.F.R. § 401 et seq. will be deemed modified as may be required to conform to the provisions of those statutes and regulations.

2.2 License to NPLH. Subject to the terms and conditions of this Agreement, Everest hereby grants to NPLH an exclusive (even as to Everest), royalty-free license under the Everest Technology solely to Exploit Licensed Products in the Licensed Field outside the Territory, with the right to grant sublicenses in accordance with Section 2.3 (Sublicense Rights).

2.3 Sublicense Rights.

(a) **Affiliates.** Subject to the terms of this Section 2.3 (Sublicense Rights), Everest may grant a sublicense of the license granted in Section 2.1 (License to Everest) through multiple tiers to Affiliates of Everest without prior notice to or the prior consent of NPLH; provided that (i) Licensed Know-How may only be sublicensed along with the Licensed Patents (other than in the case of a sublicense to a fee-for-service Subcontractor in the context of subcontracting pursuant to Section 2.9 (Subcontracting)); (ii) Everest shall cause each Affiliate to comply with the applicable terms and conditions of this Agreement, as if such Affiliate were a Party to this Agreement; and (iii) Everest shall be responsible for all actions, activities and obligations to NPLH of such Affiliate. Subject to the terms of this Section 2.3 (Sublicense

Rights), NPLH may grant a sublicense of the license granted in Section 2.2 (License to NPLH) through multiple tiers to Affiliates of NPLH without prior notice to or the prior consent of Everest; provided that (i) Everest Know-How may only be sublicensed along with the Everest Patents (other than in the case of a sublicense to a fee-for-service Subcontractor in the context of subcontracting pursuant to Section 2.9 (Subcontracting)); (ii) NPLH shall cause each Affiliate to comply with the applicable terms and conditions of this Agreement, as if such Affiliate were a Party to this Agreement; and (iii) NPLH shall be responsible for all actions, activities and obligations to Everest of such Affiliate

(b) **Third Parties.** Upon the prior written consent of NPLH, such consent not to be unreasonably withheld, conditioned, or delayed, Everest may grant a sublicense of the rights granted under the license in Section 2.1 (License to Everest) through multiple tiers to any Third Party; provided that (i) Licensed Know-How may only be sublicensed along with the Licensed Patents (other than in the case of a sublicense to a fee-for-service Subcontractor in the context of subcontracting pursuant to Section 2.9 (Subcontracting)); (ii) each sublicense granted to a Third Party shall be in writing, and shall incorporate terms and conditions that are consistent with, and expressly made subject to, the terms and conditions of this Agreement; (iii) NPLH shall be provided by Everest with a copy of such sublicense agreement within [***] days of execution, which copy may redact any financial or other proprietary terms; and (iv) Everest shall be responsible to NPLH for a breach of this Agreement due to the breach by such Third Party of such sublicense agreement. Everest hereby waives any requirement that NPLH exhaust any right, power or remedy, or proceed against any such sublicensee for any obligation or performance under this Agreement prior to proceeding directly against Everest. Upon the prior written consent of Everest, such consent not to be unreasonably withheld, conditioned, or delayed, NPLH may grant a sublicense of the rights granted under the license in Section 2.2 (License to NPLH) through multiple tiers to any Third Party; provided that (i) Everest Know-How may only be sublicensed along with the Everest Patents (other than in the case of a sublicense to a fee-for-service Subcontractor pursuant to Section 2.9 (Subcontracting)); (ii) each sublicense granted to a Third Party shall be in writing, and shall incorporate terms and conditions that are consistent with, and expressly made subject to, the terms and conditions of this Agreement; (iii) Everest shall be provided by NPLH with a copy of such sublicense agreement within [***] days of execution, which copy may redact any financial or other priority terms; and (iv) NPLH shall be responsible to Everest for a breach of this Agreement due to the breach by such Third Party of such sublicense agreement. NPLH hereby waives any requirement that Everest exhaust any right, power or remedy, or proceed against any sublicensee for any obligation or performance under this Agreement prior to proceeding directly against NPLH.

(c) A copy of each sublicense agreement with any Third Party shall, without redaction, be made available to (i) pursuant to Section 8.9 (Financial Records and Audit), any independent certified public accountant for the purpose of verifying for NPLH the accuracy of the financial reports furnished by Everest under this Agreement or of any payments made, or required to be made, by Everest to NPLH pursuant to this Agreement and (ii) pursuant to Section 8.10 (Audit Dispute), any Auditor resolving a financial disagreement between the Parties.

(d) Potentiator hereby grants to Everest an exclusive option (the "**SPR741 Option**"), exercisable by written notice from Everest to Potentiator (the "**Option Notice**")

during the period commencing on the Effective Date and ending on the first anniversary of the Effective Date (the "**Option Period**"), to negotiate a license agreement providing an exclusive (even as to Potentiator) license to the Patents and Know-How covering SPR741 in the Licensed Field in the Territory and on substantially the same terms contained herein (including, without limitation, an upfront payment, development and commercial milestones, and royalties), as further described in Section 2.12 (Option to License SPR741).

2.4 NPLH's Retained Rights; Limitations of License Grants.

(a) **Retained Rights of NPLH**. Notwithstanding anything to the contrary in this Agreement and without limitation of any rights granted or reserved to NPLH pursuant to any other term or condition of this Agreement, NPLH hereby expressly retains, on behalf of itself and its Affiliates (and on behalf of its and their direct and indirect Third Party licensors under any In-License Agreement, (sub)licensees and contractors) all right, title and interest in and to the Licensed Patents, the Licensed Know-How, NPLH Development Data, NPLH's interests in and to Joint Patents and Joint Know-How, Regulatory Documentation of NPLH and the Corporate Names of NPLH, Spero Parent and their Affiliates, in each case, for purposes of performing or exercising the Retained Rights.

(b) **In-License Agreements**

(1) If NPLH or any of its Affiliates negotiates with a Third Party at arms' length to obtain a license to Infringed IP (an "**In-License Agreement**"), then NPLH shall promptly notify Everest and identify the relevant Third Party's Infringed IP, with a copy to the JDC. The applicable Third Party's Infringed IP shall be included in the license granted to Everest under Section 2.1 (License to Everest) and considered NPLH Patents and NPLH Know-How, respectively, only if NPLH discloses the substantive terms of the In-License Agreement to Everest, which NPLH hereby agrees to do, and Everest agrees in writing to (A) comply with all the relevant obligations of such In-License Agreement, and (B) pay [***]% of all upfront, milestone, royalty and other payments applicable to the Development, Manufacture or Commercialization of the Compound or any Licensed Product in the Licensed Field in the Territory; provided, however, that, such upfront, milestone, royalty and other payments should be (x) at fair market value for such a license in the Territory; and (y) directly attributable to the Development, Manufacture or Commercialization of the Compound or any Licensed Product in the Licensed Field in the Territory, or outside the Territory for use in the Territory, by Everest or any of its Affiliates or any Sublicensees. For the avoidance of doubt, if Everest reasonably determines that such Third Party's Infringed IP under the In-License Agreement is not necessary for the Development, Manufacture or Commercialization of the Compound or any Licensed Product in the Licensed Field in the Territory, Everest has the right not to pay any costs associated with such In-License Agreement, in which case such Infringed IP shall not be included in the license granted to Everest under Section 2.1 (License to Everest) nor considered to be NPLH Patents and NPLH Know-How.

(2) If Everest or any of its Affiliates or Sublicensees negotiates with a Third Party at arms' length to obtain a license to Infringed IP, then Everest shall promptly notify NPLH and identify the relevant Third Party's Infringed IP, with a copy to the JDC. The

applicable Third Party's Infringed IP shall be included in the license granted by Everest to NPLH under Section 2.2 (License to NPLH) and considered Everest Patents and Everest Know-How, respectively, only if Everest discloses the substantive terms of such Third Party license to NPLH, which Everest hereby agrees to do, and NPLH agrees in writing to (A) comply with all the relevant obligations of such Third Party license; (B) pay [***]% of all upfront, milestone, royalty and other payments applicable to the Development, Manufacture or Commercialization of the Compound or any Licensed Product in the Licensed Field in the Territory; and (C) pay all upfront, milestone, royalty and other payments applicable to the Development, Manufacture or Commercialization of the Compound or any Licensed Product in the Licensed Field outside the Territory; provided, however, that, such upfront, milestone, royalty and other payments under clause (B) above should be (x) at fair market value for such a license in the Territory; and (y) directly attributable to the Development, Manufacture or Commercialization of the Compound or any Licensed Product in the Licensed Field in the Territory, or outside the Territory for use in the Territory, by Everest or any of its Affiliates or any Sublicensees. For the avoidance of doubt, if NPLH reasonably determines that such Third Party's Infringed IP is not necessary for the Development, Manufacture or Commercialization of the Compound or any Licensed Product in the Licensed Field outside the Territory, NPLH has the right not to pay any costs associated with such Third Party license, in which case such Infringed IP shall not be included in the license granted to NPLH under Section 2.2 (License to NPLH) nor considered to be Everest Patents and Everest Know-How. In the event that NPLH does agree to accept such Third Party license, the provisions of clauses (3), (4) and (5) of this Section 2.4(b) (In-License Agreements) shall apply, *mutatis, mutandis*, to any such Third Party license.

(3) Subject to this Section 2.4(b) (In-License Agreements), the licenses granted by NPLH in Section 2.1 (License to Everest) includes sublicenses solely under the applicable license rights granted to NPLH or its Affiliates by Third Parties under the In-License Agreements. Any Sublicense with respect to Know-How or Patents of a Third Party hereunder and any right of Everest (if any) to grant a further sublicense thereunder, shall be subject and subordinate to the terms and conditions of the In-License Agreement under which such sublicense is granted and shall be effective solely to the extent permitted under the terms of such agreement. Without limitation of the foregoing, in the event and to the extent that any In-License Agreement requires that particular terms or conditions of such In-License Agreement be contained or incorporated in any agreement granting a sublicense thereunder, such terms and conditions are hereby deemed to be incorporated herein by reference and made applicable to the sublicense granted herein under such In-License Agreement.

(4) The Parties shall cooperate with each other in good faith to support each other in complying with NPLH's and its Affiliates' obligations under each In-License Agreement. Without limitation to the foregoing, (A) the Parties shall, from time to time, upon the reasonable request of either Party, discuss the terms of an In-License Agreement and agree upon, to the extent reasonably possible, a consistent interpretation of the terms of such In-License Agreement in order to, as fully as possible, allow NPLH and its Affiliates to comply with the terms of such In-License Agreement; (B) to the extent there is a conflict between any terms of this Agreement and any terms of any In-License Agreement (including with respect to sublicensing rights, diligence obligations, prosecution, maintenance, enforcement, defense, any obligations for a counterparty to such In-License Agreement to maintain a Party's information as

confidential and any obligations for a Party to maintain as confidential the information of a counterparty to such In-License Agreement), the terms of such In-License Agreement shall control with respect to the relevant Know-How, Patents or other rights granted to Everest hereunder; and (C) Everest and its Affiliates and Sublicensees shall comply with any applicable reporting and other requirements under the In-License Agreements, and the provisions regarding currency conversion, international payments and late payments, and any other relevant definitions and provisions, of the relevant In-License Agreements shall apply to the calculation of the payments due under the relevant In-License Agreements.

(5) On an In-License Agreement-by-In-License Agreement basis, from and after the date on which Everest agrees in writing pursuant to Section 2.4(b)(1) to accept the Patents and Know-How covered by such In-License Agreement as Licensed Technology under this Agreement, NPLH shall not enter into any subsequent agreement with any other party to such In-License Agreement that modifies or amends such In-License Agreement in any way that would materially adversely affect Everest's rights or interest under this Agreement without Everest's prior written consent, which shall not be unreasonably withheld, conditioned or delayed, and shall provide Everest with a copy of all modifications to or amendments of such In-License Agreement, regardless of whether Everest's consent was required with respect thereto.

2.5 Initial Transfer of Know-How. Upon the written request of Everest, NPLH shall commence disclosing and making available to Everest the Licensed Know-How (including the NPLH Development Data therein) necessary or reasonably required for Everest to file a CTA covering a Licensed Product. Such disclosure and transfer shall be made according to a timeline mutually agreed by Everest and NPLH, each of which shall cooperate with each other in good faith to enable a smooth transfer of the Licensed Know-How from NPLH to Everest. Upon Everest's reasonable request during such transfer, NPLH shall provide reasonable technical assistance, including making appropriate employees available to Everest at reasonable times, places and frequency, and upon reasonable prior notice, for the purpose of assisting Everest to understand and use the Licensed Know-How in connection with Everest's filing of such CTA covering such Licensed Product. NPLH shall be responsible for only the costs associated with the first [***] FTE hours of activities by such employees and advisors under this Section 2.5 and the activities described in Section 6.2 and (ii) Everest shall be responsible for any costs and expenses of any such activities under this Section 2.5 and Section 6.2 once such [***]-FTE threshold is used, and shall pay or reimburse NPLH at the Reimbursement Rate following a written invoice in reasonable detail.

2.6 No Implied Licenses; Negative Covenant. Except as set forth herein, no Party shall acquire any license or other intellectual property interest, by implication or otherwise, under any Know-How, Patents, trademarks or other intellectual property rights owned or Controlled by any other Party. Everest hereby covenants not to practice, and not to permit or cause any of its Affiliates or any Third Party to practice, any Licensed Technology for any purpose other than as expressly authorized in this Agreement.

2.7 Non-Diversion. Everest hereby covenants and agrees that it will not, and will ensure that its Affiliates will not, and will ensure its Sublicensees and subcontractors are bound by contractual obligations not to, either directly or indirectly, promote, market, solicit, distribute,

import, sell or have sold Licensed Products outside the Territory. In furtherance of the foregoing, Everest shall not and will ensure that its Affiliates do not, and shall use Commercially Reasonable Efforts to ensure that its or their Sublicensees or distributors do not knowingly distribute, market, promote, offer for sale or sell the Compound or any Licensed Product directly or indirectly to any Person outside the Territory or to any Person inside the Territory that Everest or any of its Affiliates or any of its or their Sublicensees or distributors knows has directly or indirectly distributed, marketed, promoted, offered for sale or sold, or has reasonable grounds to believe intends to directly or indirectly distribute, market, promote, offer for sale or sell, the Compound or any Licensed Product for use outside the Territory. If Everest or any of its Affiliates receives or becomes aware of the receipt by it or any Sublicensee or distributor of any orders for the Compound or any Licensed Product for use outside the Territory, such Person shall refer such orders to NPLH.

2.8 Non-Compete. During the Term of this Agreement, Everest shall not, and shall cause its Affiliates and their respective Sublicensees, not to, directly or indirectly, enable or assist any Person that is not a Party to this Agreement to, Develop, Manufacture or Commercialize any polymyxin-based compound, or fund any such activities, that [***] (collectively, "**Polymyxin Class Compounds**"), whether alone or in combination with other compounds, for any intravenous indication in the Licensed Field, other than the Compound and the Licensed Products in accordance with this Agreement. If Everest requests a waiver of this Section 2.8 with regard to a particular Polymyxin Class Compound and/or a particular transaction, NPLH will in good faith give due consideration to such request. Notwithstanding the foregoing, (a) if Everest exercises the SPR741 Option and executes and delivers a license agreement with Potentiator providing an exclusive license to the Patents and Know-How covering SPR741, or (b) Everest is acquired by a Third Party that, at the time of such acquisition, is actively Developing, Manufacturing and/or Commercializing any Polymyxin Class Compounds (whether in or outside the Territory), then the activities of Everest, its Affiliates and their respective Sublicensees under and in accordance with the terms of such license agreement and the activities of such Third Party acquirer, respectively, shall not be deemed to breach this Section 2.8.

2.9 Subcontracting. Subject to Section 2.3 (Sublicense Rights), Everest may subcontract on a fee-for-service basis with a Third Party to perform any or all of its obligations hereunder (a "**Subcontractor**"), including by appointing one or more distributors; provided that (a) no such permitted subcontracting shall relieve Everest of any obligation hereunder (except to the extent satisfactorily performed by such Subcontractor) or any liability and Everest shall be and remain fully responsible and liable therefor; (b) the agreement pursuant to which Everest engages any Subcontractor must be consistent in all material respects with this Agreement, including terms consistent with the confidentiality, restrictions on use and intellectual property provisions of this Agreement, and (c) Everest shall be responsible to NPLH for the breach of this Agreement due to breach of any subcontracting agreement by its Subcontractors. Everest hereby waives any requirement that NPLH exhaust any right, power or remedy, or proceed against any Subcontractor for any obligation or performance under this Agreement prior to proceeding directly against Everest.

2.10 Statements and Compliance with Applicable Laws. Everest shall and shall cause its Affiliates and its and their respective Sublicensee's to comply with all Applicable Laws with respect to the Exploitation of Licensed Products. Everest shall, and shall cause its Affiliates to, and shall use Commercially Reasonable Efforts to cause its and their Sublicensees, employees, representatives, agents, and distributors to avoid taking, or failing to take, any actions that Everest knows or reasonably should know would jeopardize the goodwill or reputation of NPLH or its Affiliates or the Licensed Products or any Trademark associated therewith. Without limitation to the foregoing, Everest shall in all material respects conform its practices and procedures relating to the Commercialization of the Licensed Products and educating the medical community in the Territory with respect to the Licensed Products to any applicable industry association regulations, policies and guidelines, as the same may be amended from time to time, and Applicable Laws. Everest agrees that in performing its obligations under this Agreement, it will not employ or engage any Person who has been debarred or disqualified by any Regulatory Authority, or, to its knowledge, is the subject of debarment or disqualification proceedings by a Regulatory Authority.

2.11 Section 365(n). All rights and licenses granted under or pursuant to this Agreement by NPLH or Everest are, and will otherwise be deemed to be, for the purposes of Section 365(n) of the U.S. Bankruptcy Code, and any similar law in the Territory, licenses of rights to "intellectual property" as defined under Section 101 of the U.S. Bankruptcy Code or any similar law in the Territory. The Parties agree that the Parties, as licensees of such rights under this Agreement, will retain and may fully exercise all of their rights and elections under the U.S. Bankruptcy Code or any similar law in the Territory. The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against either Party under the U.S. Bankruptcy Code or any similar law in the Territory, the Party that is not a party to such proceeding will be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property and all embodiments of such intellectual property, and same, if not already in their possession, will be promptly delivered to them (a) upon any such commencement of a bankruptcy proceeding upon their written request therefor, unless the Party subject to such proceeding elects to continue to perform all of its obligations under this Agreement, or (b) if not delivered under (a) above, following the rejection of this Agreement by or on behalf of the Party subject to such proceeding upon written request therefor by the non-subject party.

2.12 Option to License SPR741.

(a) As consideration for the SPR741 Option, Everest shall pay Potentiator within [***] Business Days after the Effective Date, a one-time, non-refundable option fee of one million Dollars ($1,000,000) (the "**Option Fee**"), which Option Fee, if paid, shall be creditable against the one-time, non-refundable and non-creditable upfront payment required to be paid by Everest to Potentiator under such license agreement, if entered into.

(b) If Everest exercises the SPR741 Option during the Option Period, then Potentiator and Everest shall negotiate a license agreement for such exclusive license in good faith for a period of not more than [***] days, provided that such period may be further extended by the relevant Parties' mutual written consent. Potentiator hereby agrees not to assign, transfer or otherwise provide an option to license the Patents and Know-How covering SPR741 in the

Territory until the later of (i) the expiration of such [***] day period (or such longer period as mutually agreed by the relevant Parties) or (ii) [***] year anniversary of the Effective Date. If Everest does not exercise the SPR741 Option, or the relevant Parties fail to execute and deliver such license agreement at the end of such [***] day period (or such longer period as mutually agreed by the relevant Parties), Potentiator shall have no future obligations with respect to the SPR741 Option or the Patents and Know-How covering SPR741.

ARTICLE 3
GOVERNANCE

3.1 Joint Development Committee. Within [***] days after the Effective Date, the Parties shall establish a joint development committee (the "**Joint Development Committee**" or the "**JDC**"), composed of [***] representatives of NPLH (if NPLH elects to participate) and [***] representatives of Everest, to coordinate the Development and Commercialization of the Compound and Licensed Products in the Licensed Field in the Territory. Each JDC representative shall have appropriate knowledge and expertise and sufficient seniority within the applicable Party to make decisions arising within the scope of the JDC's responsibilities. For the purposes of participation in the JDC, NPLH has the right but not the obligation to participate in the JDC. The JDC shall:

(a) serve as a forum for discussing Development of the Compound and Licensed Products in the Licensed Field in the Territory, including by reviewing the Development Plan and coordinating the conduct of the Development activities;

(b) serve as a forum for discussing the Commercialization of Licensed Products in the Licensed Field in the Territory, including by reviewing the Commercialization strategy for the Territory, reviewing the Commercialization Plans and coordinating the conduct of the Commercialization activities;

(c) serve as a forum for discussing the Manufacture and supply of Compound and Licensed Products in the Licensed Field in the Territory, including by reviewing the Development strategy and Commercialization strategy for the Territory and coordinating the conduct of the Manufacturing and supply activities;

(d) serve as a forum for discussing and supervising Development of the Compound and Licensed Products in the Licensed Field in the Territory, including by (i) providing Everest with a forum at each meeting to disclose Everest's, or its Affiliates' or Sublicensees' activities with respect to achieving Regulatory Approvals of Licensed Products in the Territory; material clinical study results; and the Marketing Authorization Applications that Everest or any of its Affiliates reasonably expect to make, seek or attempt to obtain in the Territory; (ii) reviewing the current Development Plan and, with the JDC's approval, making any amendments or updates to the Development Plan; and (iii) coordinating the conduct of the Development activities;

(e) serve as a forum at each meeting for discussing and supervising the Commercialization of Licensed Products in the Licensed Field in the Territory, including by (i) providing Everest with a forum to disclose to Everest's, or its Affiliates' or Sublicensees'

Commercialization activities with respect to Licensed Products in the Territory; (ii) reviewing the Commercialization strategy for the Territory; (iii) reviewing the Commercialization Plan and, with the JDC's approval, making any amendments or updates to the Commercialization Plan; and (iv) coordinating the conduct of the Commercialization activities;

(f) coordinate the activities of NPLH and Everest under this Agreement; and

(g) perform such other functions as are set forth herein or as the Parties may mutually agree in writing, except where in conflict with any provision of this Agreement.

The JDC shall have only such powers as are expressly assigned to it in this Agreement, and such powers shall be subject to the terms and conditions of this Agreement. For clarity, the JDC shall not have any right, power or authority: (i) to receive the Option Notice or negotiate the execution and delivery of a license agreement under the Patents and Know-How covering SPR741, or review or make any termination under any such license agreement; (ii) determine any issue in a manner that would conflict with the express terms and conditions of this Agreement; or (iii) to modify or amend the terms and conditions of this Agreement.

3.2 JDC Membership and Meetings.

(a) **JDC Members.** NPLH's initial JDC representatives will be [***] and Everest's initial JDC representatives will be [***]. The chairmanship for each meeting shall rotate between NPLH and Everest, with one of each Party's JDC representatives acting as chairperson of the JDC on a rotating basis. Each Party may replace its JDC representatives on written notice to the other Party, but each Party shall strive to maintain continuity. The JDC members shall jointly prepare and circulate the meeting agenda at least [***] Business Days in advance of each meeting, and shall also promptly, but in no event later than [***] days after such meeting, prepare and circulate for review and approval of the Parties the minutes of such meeting.

(b) **JDC Meetings.** The JDC will hold its first meeting within [***] days of establishment of the JDC pursuant to Section 3.1 (Joint Development Committee). At this first meeting, the JDC will address the initial transfer of Licensed Know-How provided for in Section 2.5 (Initial Transfer of Know-How) and any other topics the Parties deem appropriate. Thereafter, the JDC shall hold meetings at such times as it elects to do so, but in no event shall such meetings be held less frequently than [***] per Calendar Year. Meetings may be held in person, or by audio or video teleconference; provided, that unless otherwise agreed by NPLH and Everest, at least [***] meeting per year shall be held in person, and all in-person JDC meetings shall be held at locations mutually agreed upon by NPLH and Everest. Each Party shall be responsible for all of its own expenses of participating in JDC meetings.

(c) **Non-Member Attendance.** Each of NPLH and Everest may from time to time invite a reasonable number of participants, in addition to its representatives, to attend JDC meetings in a non-voting capacity; provided, that if either NPLH or Everest intends to have any Third Party (including any consultant) attend such a meeting, such Party shall provide at least [***] days prior written notice to the other Party and obtain the other Party's approval for such Third Party to attend such meeting, which approval shall not be unreasonably withheld or

delayed. Such Party shall ensure that such Third Party is bound by confidentiality and non-use obligations consistent with the terms of this Agreement, and provide the other Party with a copy of such confidentiality agreement. The Party inviting any such Third Party shall be responsible for all of such Third Party's costs and expenses of participating in JDC meetings, unless such invitation is mutually made by NPLH and Everest, in which case they shall equally share such costs and expenses.

3.3 JDC Decision-Making. All decisions of the JDC shall be made by unanimous vote, with NPLH's representatives and Everest's representatives each collectively having [***] vote. If after reasonable discussion and good faith consideration of each of their views on a particular matter before the JDC, the representatives of NPLH and Everest cannot reach an agreement as to such matter within [***] Business Days after such matter was brought to the JDC for resolution, such disagreement shall:

(a) be referred to the Chief Executive Officer of Spero Parent (or his or her designee) and the Chief Executive Officer of Everest (or his or her designee) (collectively, the "**Executive Officers**") for resolution, who shall use good faith efforts to resolve such matter within [***] Business Days after it is referred to them and, if such matter is resolved by the Executive Officers, such resolution shall be implemented by and binding on the Parties.

(b) If the Executive Officers are unable to reach consensus on any such matter during such [***] Business Day period, then (i) the Chief Executive Officer of Everest shall have the right to make the final decision if such matter (A) involves the Development of, Regulatory Approval for, Commercialization or other Exploitation of the Compound or a Licensed Product solely in the Territory and (B) does not involve NPLH's Retained Rights and could not reasonably be expected to have a material adverse effect on the Development of, Regulatory Approval for, Commercialization or Exploitation of the Compound or a Licensed Product outside the Territory; (ii) the Chief Executive Officer of Spero Parent shall have the right to make the final decision if such matter either (A) involves the Development of, Regulatory Approval for, Commercialization or other Exploitation of the Compound or a Licensed Product solely outside the Territory, or NPLH's Retained Rights, or (B) involves the Development of, Regulatory Approval for, or Commercialization or other Exploitation of the Compound or a Licensed Product in the Territory but could reasonably be expected to have a material adverse effect on the Development of, Regulatory Approval for, or Commercialization or Exploitation of the Compound or a Licensed Product outside the Territory; or (iii) in all other cases, such matter will be resolved in accordance with Section 14.10 (Dispute Resolution).

(c) If NPLH does not participate in establishing the JDC or appoint members to the JDC, Everest shall have the votes and the decision-making power of NPLH with respect to the JDC unless and until NPLH appoints members to the JDC.

ARTICLE 4
DEVELOPMENT

4.1 General. Subject to the terms and conditions of this Agreement (including without limitation the Retained Rights), Everest shall be solely responsible for the Development

of the Compound and Licensed Products in the Licensed Field in the Territory, including the performance of preclinical and clinical studies of any Compound or any Licensed Product in the Licensed Field in the Territory, all in accordance with the Development Plan.

4.2 Development Plan. Everest shall conduct all Development of the Compound and Licensed Products in the Licensed Field in the Territory in accordance with a comprehensive development plan, the initial version of which is attached to this Agreement as Exhibit E (the "**Initial Development Plan**", and as amended from time to time in accordance with this Agreement, the "**Development Plan**"). The Development Plan will include, among other things, the indications for which a Licensed Product is to be Developed and other exploratory indications for which a Licensed Product may be developed, critical activities to be undertaken, certain timelines, go/no go decision points and relevant decision criteria and certain allocations of responsibilities between the Parties for the various activities to be undertaken under the Development Plan. The Development Plan will be focused on efficiently obtaining Regulatory Approval for a Licensed Product in the Licensed Field in the Territory while taking into consideration Development, Regulatory Approval, or commercial impacts on the Licensed Product outside the Licensed Field and Territory. From time to time, but at least [***] per Calendar Year, the Parties will, with the assistance of the JDC, update the Development Plan and submit such updated plan to the JDC for review, discussion, and approval. The then-current Development Plan will at all times contain at least that level of detail and cover at least the same matters (to the extent applicable) as the Initial Development Plan. If any updated Development Plan is not approved by the JDC, any disagreement or dispute shall be resolved by the JDC in the manner set forth in Section 3.3 (JDC Decision-Making). If any updated or new terms of the Development Plan contradict, or create inconsistencies or ambiguities with, the terms of this Agreement, then the terms of this Agreement shall govern.

4.3 Diligence.

(a) **Commercially Reasonable Efforts**. Everest, directly and/or with or through its Affiliates or Sublicensees, shall use Commercially Reasonable Efforts to Develop, Exploit, Commercialize and obtain Regulatory Approval for the Compound and each Licensed Product in the Licensed Field in the Territory in accordance with the Development Plan and the Commercialization Plan.

(b) **Specific Diligence Events**. In furtherance of Section 4.3(a) (Commercially Reasonable Efforts) and without limitation thereof, Everest shall use Commercially Reasonable Efforts to achieve, by itself or through its Affiliates or Sublicensees, the following diligence milestones (each, a "**Diligence Milestone**") with respect to the Compound and a Licensed Product in each case on or prior to the applicable target date (the "**Diligence Target Dates**"):

(1) File a CTA in the Territory for a Licensed Product within [***] years after the Effective Date;

(2) Initiate a Phase 3 Clinical Trial in the Territory for a Licensed Product within [***] years after the Effective Date; and

(3) First filing of an NDA covering a Licensed Product in Mainland China within [***] years after the Effective Date.

If Everest reasonably believes that it will not achieve a Diligence Milestone on or prior to the applicable Diligence Target Date, Everest shall notify NPLH in writing as far in advance of the applicable Diligence Target Date as reasonably practicable (a "**First Diligence Notice**"), which First Diligence Notice shall address the reasons for not timely achieving the relevant Diligence Milestone (including whether there is any reason constituting a "force majeure" as described in Section 14.6 (Force Majeure), the efforts Everest is continuing to expend toward meeting such Diligence Milestone and suggesting a reasonable extension to such Diligence Target Date for achieving such Diligence Milestone. Within [***] days following receipt of a First Diligence Notice, NPLH may inform Everest in writing that either (i) NPLH accepts the provisions of such First Diligence Notice (which NPLH shall do in the event that the delay is attributable to a reason of "force majeure"), in which case the Parties agree to promptly amend this Section 4.3(b) (Specific Diligence Events) to incorporate a new mutually agreed Diligence Target Date or (ii) NPLH desires to have further discussions with Everest concerning such Diligence Milestone and the efforts of Everest to achieve such Diligence Milestone, in which case, within [***] Business Days following receipt of such notice from NPLH, the Executive Officers of each Party shall set a date within the following [***] days (the "**Diligence Meeting Date**") for a meeting (a "**Diligence Meeting**"), at which Diligence Meeting each Party shall present its views concerning, and evidence (if applicable) as to, whether Everest has used and will continue to use Commercially Reasonable Efforts to achieve such Diligence Milestone, together with any other relevant information. If the Parties are able reach agreement at such Diligence Meeting as to modifications to this Section 4.3(b) (Specific Diligence Events), then the Parties shall promptly amend this Agreement accordingly. If the Parties are unable to reach agreement at such Diligence Meeting, then Everest shall have [***] days to achieve such Diligence Milestone or to demonstrate, to the reasonable satisfaction of NPLH, that it has continually used Commercially Reasonable Efforts to achieve such Diligence Milestone. If, following such [***] day period, Everest has still not achieved such Diligence Milestone or demonstrated, to the reasonable satisfaction of NPLH, that it has continually used Commercially Reasonable Efforts to achieve such Diligence Milestone, then, in addition to any other rights or remedies available to NPLH, NPLH may initiate termination of this Agreement pursuant to Section 11.2(c) (Termination for Cause) of this Agreement.

4.4 Development Costs.

(a) As between the Parties, Everest shall be solely responsible for the cost for the Development of the Compound and the Licensed Products in the Licensed Field in the Territory and NPLH shall be solely responsible for the cost for the Development of the Compound and the Licensed Products in the Licensed Field outside the Territory.

(b) If NPLH (or its sublicensee) and Everest cooperate on any multi-regional clinical trial conducted both inside and outside the Territory, then Everest shall (i) be responsible for all direct costs and expenses of conducting such clinical trial in the Territory and (ii) pay or reimburse NPLH for a pro rata portion of all of the Indirect Costs of such multi-regional clinical trial, not to exceed [***] percent ([***]%) of the total Indirect Costs of such multi-regional

clinical trial. For clarity, this subsection (b) shall not apply to the initial Milestone Event, [***], which shall be reimbursed through Everest's payment of the corresponding Milestone Payment.

(c) If, at the request of NPLH (or its sublicensee), Everest agrees to assist NPLH (or its sublicensee) in Development beyond the scope of Everest's obligations under this Agreement (for example, Development outside the Territory or Development in the Territory for a multi-regional clinical trial for an indication of the Licensed Product that Everest is not interested in Developing in the Territory), then NPLH shall pay or reimburse Everest all costs and expenses for such assistance, including Everest's employee costs at the Reimbursement Rate and Third Party expenses as actually incurred.

4.5 Development Records and Report.

(a) Everest shall, and shall cause its Affiliates and its and their Sublicensees to, maintain, in good scientific manner, complete and accurate books and records pertaining to Development of Licensed Products hereunder, in sufficient detail for NPLH to verify Everest's compliance with its obligations under this Agreement. Such books and records shall (i) be summarized in English in sufficient detail for NPLH to verify Everest's compliance with its obligations under this Agreement and for NPLH to properly use such books and records for patent and regulatory purposes, (ii) be appropriate for patent and regulatory purposes; (iii) be in compliance with Applicable Laws; (iv) properly reflect all work done and results achieved in the performance of its Development activities hereunder; (v) record only such activities and not include or be commingled with records of activities outside the scope of this Agreement; and (vi) be retained by Everest for at least [***] years after the expiration or termination of this Agreement in its entirety or for such longer period as may be required by Applicable Laws.

(b) On [***] of each year starting from the year of [***], each of Everest and NPLH shall provide the other Party with a written report summarizing in sufficient detail for NPLH to verify Everest's compliance with its obligations under this Agreement (i) the Development activities conducted in the preceding Calendar Year by it and its Affiliates and Sublicensees, and (ii) the Development activities planned to be conducted in such Calendar Year by it and its Affiliates and Sublicensees. If at any time a Party's representatives on the JDC are not fully able to perform their rights and duties on the JDC in the absence of a review of any of such books and records, the other Party shall, upon reasonable written request from such JDC representative, provide a copy of such records to the JDC.

ARTICLE 5
REGULATORY

5.1 Regulatory Responsibilities. Everest shall be responsible, at its cost and subject to the Retained Rights and except as set forth in this ARTICLE 5, for all regulatory activities necessary to prepare, obtain and maintain Marketing Authorization Applications, Regulatory Filings and other Regulatory Approvals for the Compound and Licensed Products in the Licensed Field in the Territory. Everest shall keep NPLH informed of regulatory developments related to the Compound and Licensed Products in the Licensed Field in the Territory via the JDC.

5.2 Regulatory Reports. On [***] of each year starting from the year of [***], each of Everest and NPLH shall provide the other Party with a written report summarizing the clinical data and safety results generated from the regulatory activities performed in the preceding Calendar Year by it and its Affiliates and Sublicensees, in sufficient detail for NPLH to verify Everest's compliance with its obligations under this Agreement and for NPLH to properly use data and results for patent and regulatory purposes.

5.3 Regulatory Cooperation.

(a) **Everest.** Everest shall notify NPLH of all material Regulatory Documentation submitted or received by Everest or its Affiliates or Sublicensees that are related to any Licensed Product in the Territory reasonably prior to such submission or reasonably after receipt. Moreover, with respect to Regulatory Filings in the Territory, Everest will provide NPLH with (i) an English summary of such draft filings and (ii) an English translation of that portion of the draft filings newly developed and prepared by Everest reasonably prior to submission so that NPLH may have sufficient opportunity to review and comment on them. Everest shall consider all comments of NPLH in good faith, taking into account the best interests of the Development, Regulatory Approval and/or Commercialization of the Licensed Product, but has no obligation to accept any comments of NPLH, except to the extent that ignoring such comment could reasonably be expected to have a material adverse effect on the Development of, Regulatory Approval for, or Commercialization or Exploitation of the Compound or a Licensed Product outside the Territory, or on NPLH's Retained Rights. Material submissions made by Everest to, or correspondence with, Regulatory Authorities will be provided to NPLH sufficiently in advance to enable translation by NPLH, if any such submissions or correspondence are not available in English. NPLH shall not provide any Regulatory Documentation of Everest, its Affiliates, or Sublicensees to any of NPLH's sublicensees who does not agree pursuant to Section 5.3(b) (NPLH) to permit its Regulatory Documentation to be shared with Everest, its Affiliates, and its Sublicensees.

(b) **NPLH.** NPLH shall provide or make available to Everest copies of all material Regulatory Documentation submitted or received by NPLH or its Affiliates that are related to any Licensed Product outside the Territory reasonably after such submission or receipt. NPLH shall use Commercially Reasonable Efforts to negotiate an agreement with each sublicensee to make available to Everest copies of all material Regulatory Documentation that are related to any Licensed Product outside the Territory that are Controlled by its such sublicensee.

(c) **Confidentiality.** Any information of a Party to which the other Party obtains access pursuant to this Section 5.3 (Regulatory Cooperation) shall, subject to ARTICLE 10 (Confidentiality; Publication), be deemed the Confidential Information of such first Party.

(d) **Discontinuation**. In the event that Everest (including its Affiliates and their respective Sublicensees) discontinues Development or Commercialization of any Licensed Product in the Territory, then (1) the license of NPLH Licensed Technology to Everest under Section 2.1 (License to Everest) as to such Licensed Product shall be terminated; (2) Everest shall, at its expense, return all NPLH Development Data and NPLH Regulatory Documentation

to NPLH, as well as transfer to NPLH any Everest Development Data and Everest Regulatory Documentation related to the discontinued Licensed Product; and (3) with respect to any Everest Technology, Everest Development Data, and Everest Regulatory Documentation covering such discontinued Licensed Product, Everest shall grant a license to NPLH and the provisions of Section 11.3(d) shall apply mutatis mutandis.

5.4 Rights of Reference. Solely to the extent Regulatory Authorities in the applicable jurisdiction are permitted under Applicable Laws to utilize Regulatory Documentation submitted to Regulatory Authorities outside of the Territory:

(a) Without any additional consideration to NPLH, NPLH hereby grants to Everest and its Sublicensees a Right of Reference and Use, as that term is defined in 21 C.F.R. § 314.3(b) and any foreign counterpart to such regulation, to all NPLH Regulatory Documentation and the NPLH Development Data to the extent necessary or reasonably useful for Everest to Develop, Manufacture, obtain Regulatory Approval of, or Commercialize the Compound or Licensed Products in the Licensed Field in the Territory, in each case, pursuant to the Development Plan or Commercialization Plan and otherwise subject to the terms and conditions of this Agreement.

(b) Without any additional consideration to Everest, Everest hereby grants to NPLH and its Affiliates, and any current or future direct or indirect (sub)licensee of NPLH with respect to the Compound or a Licensed Product, a Right of Reference and Use, as that term is defined in 21 C.F.R. § 314.3(b) and any foreign counterpart to such regulation, to the Everest Development Data to the extent (i) necessary or reasonably useful for NPLH to Exploit the Compound, Licensed Product(s) or any product containing the Compound outside of the Territory, or (ii) in support of NPLH's Development, Manufacturing, Regulatory Approval, or Commercialization of the Compound, Licensed Product(s) or any product containing the Compound outside of the Territory.

(c) Promptly after Everest, its Affiliate or its or their Sublicensees generate(s) any Everest Development Data, Everest shall provide NPLH with copies of such Everest Development Data and Everest hereby grants to NPLH an exclusive (even as to Everest), royalty-free license under and to such Everest Development Data solely to Exploit Licensed Products in the Licensed Field outside the Territory, with the right to grant Sublicenses in accordance with Section 2.3 (Sublicense Rights)

(d) Each Party will provide a signed statement to this effect, if requested by the other Party, 21 C.F.R. § 314.50(g)(3) or any foreign counterpart to such regulation, in the case of a request by either Party, for the limited purpose described in this Section 5.4 (Rights of Reference).

(e) Other than as expressly set forth in this Section 5.4 (Rights of Reference), nothing in this Section 5.4 shall require either Party to take, or forbear to take, any action.

(f) Any information of a Party to which the other Party obtains access pursuant to this Section 5.4 (Rights of Reference) shall, subject to Sections 10.1 (Duty of Confidence) and 10.2 (Exceptions), be deemed the Confidential Information of such first Party.

For avoidance of doubt, a Party's submission of information of the other Party to which such Party obtains access pursuant to this Section 5.4 (Rights of Reference) to a Regulatory Authority shall be governed by and subject to the terms of ARTICLE 10 (Confidentiality; Publication).

5.5 Recalls, Suspensions or Withdrawals. Everest shall notify NPLH promptly following its determination that any event, incident or circumstance has occurred that would reasonably be expected to result in the need for a recall, market suspension or market withdrawal of a Licensed Product in the Licensed Field in the Territory and shall include in such notice the reasoning behind such determination and any supporting facts. As between the Parties, Everest shall have the right to make the final determination whether to voluntarily implement any such recall, market suspension or market withdrawal in the Licensed Field in the Territory; provided that prior to any implementation of such a recall, market suspension or market withdrawal, Everest shall consult with NPLH and shall consider NPLH's comments in good faith. If a recall, market suspension or market withdrawal is mandated by a Regulatory Authority in the Territory, as between the Parties, Everest shall initiate such a recall, market suspension or market withdrawal in compliance with Applicable Laws. For all recalls, market suspensions or market withdrawals undertaken pursuant to this Section 5.5 (Recalls, Suspensions or Withdrawals), as between the Parties, Everest shall be solely responsible for the execution thereof. Subject to ARTICLE 13 (Indemnification; Liability), Everest shall be responsible for all costs and expenses of any such recall, market suspension or market withdrawal.

5.6 Pharmacovigilance Agreement; Global Safety Database. The Parties shall enter into a pharmacovigilance agreement at least [***] days prior to the initiation of Phase 1 Clinical Trial by Everest in the Territory providing for the terms pursuant to which (i) NPLH shall establish, hold and maintain (at NPLH's sole cost and expense) the global safety database for Licensed Products and (ii) Everest shall timely provide NPLH with information in the possession and Control of Everest as necessary for NPLH to comply with its pharmacovigilance responsibilities outside the Territory, including, as applicable, any adverse drug experiences (including those events or experiences that are required to be reported to the FDA under 21 C.F.R. sections 312.32 or 314.80 or to foreign Regulatory Authorities under corresponding Applicable Laws outside the United States), from pre-clinical or clinical laboratory, animal toxicology and pharmacology studies, clinical studies and commercial experiences with a Licensed Product, in each case, in English, in the form reasonably requested by NPLH and at Everest's sole cost and expense.

5.7 Regulatory Inspections. If any Regulatory Authority (i) contacts Everest, its Affiliates or their respective Sublicensees with respect to the alleged improper Development, Manufacture or Commercialization of any Licensed Product; (ii) conducts, or gives notice of its intent to conduct, an inspection at Everest's, its Affiliate's or Sublicensee's facilities used in the Development or Manufacturing of Licensed Products or (iii) takes, or gives notice of its intent to take, any other regulatory action with respect to any activity of Everest, its Affiliates or Sublicensees that could reasonably be expected to materially adversely affect any Development, Manufacture or Commercialization activities with respect to the Licensed Product, whether in or outside the Territory, then Everest will promptly notify NPLH of such contact, inspection or notice.

ARTICLE 6
SUPPLY; MANUFACTURING

6.1 Supply Agreement.

(a) **Initial Supply Agreement**. NPLH and Everest agree to negotiate in good faith within [***] days after the Effective Date a new agreement concerning the short-term supply of the Compound for Everest's Development use (including preclinical (e.g., MIC testing) and/or clinical use) (the "**Initial Supply Agreement**"), with Everest's cost of the Compound under the Initial Supply Agreement being equal to [***]. Everest shall provide written notice to NPLH with rolling forecasts (at least quarterly) promptly following its decision on initiating pre-clinical experiments or clinical trials. Notwithstanding the foregoing, nothing in this Agreement nor the Initial Supply Agreement shall restrict, impair or otherwise limit NPLH's ability to manufacture the Compound or Licensed Products in the Territory for use outside the Territory.

(b) **Commercial Supply Agreement**. NPLH and Everest agree to negotiate in good faith within [***] days of the initiation of the first Phase 3 Clinical Trial in the Territory a new agreement concerning the supply of the Compound and/or the Licensed Product for Everest's Commercialization use (the "**Commercial Supply Agreement**"), with Everest's cost of the Compound and/or the Licensed Product under the Commercial Supply Agreement being equal to [***]. Notwithstanding the foregoing, nothing in this Agreement nor the Commercial Supply Agreement shall restrict, impair or otherwise limit NPLH's ability to manufacture the Compound or Licensed Products in the Territory for use outside the Territory.

6.2 Manufacturing Technology Transfer. In order to enable Everest to Manufacture or have Manufactured the Compound and Licensed Products consistent with the terms of Section 6.3 (Manufacturing Responsibilities), upon a written request from Everest, NPLH shall perform or facilitate technology transfer to Everest as follows: during a mutually agreed time period of no more than [***] days (the "**Manufacturing Transfer Period**"), NPLH shall (a) make available and transfer to Everest, copies of existing embodiments of the Licensed Know-How in NPLH's possession that are necessary or reasonably useful in the Manufacture of the Compound and Licensed Products and as of such date are being used by NPLH to Manufacture the Compound and Licensed Products (the "**Licensed Manufacturing Know-How**") solely for Everest and/or its Subcontractor to Manufacture the Compound and Licensed Products in accordance with the terms and conditions of this Agreement; (b) identify in writing all Subcontractors who Manufacture Compounds or Licensed Products for NPLH (each, an "**NPLH CMO**"); and (c) provide technical assistance (both on site and otherwise) in the transfer and demonstration of the Licensed Manufacturing Know-How that is necessary to Manufacture the Compound and Licensed Products. To the extent that any Licensed Manufacturing Know-How is in the Control of NPLH but is in the possession of a NPLH CMO (and is not in NPLH's possession), then during the Manufacturing Transfer Period, upon Everest's request, NPLH will use Commercially Reasonable Efforts to facilitate the transfer of such Licensed Manufacturing Know-How from such NPLH CMO to Everest, and/or cause such NPLH CMO to make such Licensed Manufacturing Know-How available to Everest, at Everest's cost. Everest, in its sole discretion and at its sole expense, may contract with any such NPLH CMO for technical

assistance (both on site and otherwise) in the transfer and demonstration of the Licensed Manufacturing Know-How that is necessary to Manufacture the Compound and Licensed Products. After the Manufacturing Transfer Period, if requested by Everest, NPLH will in good faith endeavor to provide additional technical assistance in the transfer of Licensed Manufacturing Know-How to Everest. For all activities or assistance provided by NPLH employees or advisors to Everest under this Section 6.2 or under Section 2.5, (i) NPLH shall be responsible for only the costs associated with the first [***] FTE hours of activities by such employees and advisors and (ii) Everest shall be responsible for the costs and expenses of any such activities under this Section 6.2 and Section 2.5 once such [***]-FTE threshold is used, and shall pay or reimburse NPLH at the Reimbursement Rate following a written invoice in reasonable detail.

6.3 Manufacturing Responsibilities. Everest shall have the right to Manufacture the Compound and Licensed Products inside the Territory, or outside the Territory but solely for Development and Commercialization of the Compound in the Territory under this Agreement, at its sole expense. Everest may conduct such manufacturing activities itself, through a NPLH CMO, or through another Subcontractor subject to Section 2.9 (Subcontracting). Upon request from Everest, NPLH will arrange for any NPLH CMO to discuss the Manufacture and supply of the Compound and/or Licensed Products for Everest. If, at any time, Everest elects to Manufacture the Compound or Licensed Products itself or to use a Subcontractor (including a NPLH CMO), then Everest will use product and manufacturing specifications and impose quality controls and assurances on itself or on such NPLH CMO or such Subcontractor that are at least as stringent as those used required by NPLH of its NPLH CMOs and are reasonably acceptable to NPLH. Everest may also request that an NPLH CMO Manufacture the Compound and/or Licensed Products required by Everest for preclinical and clinical use in the Territory under this Agreement, Manufactured under product and manufacturing specifications and quality controls and assurances that are at least as stringent as those used required by NPLH with such NPLH CMO. If Everest, its Affiliates, Sublicensees Manufacture, or use a Subcontractor or CMO (including a NPLH CMO) that Manufactures, a batch of API or drug product that does not meet such specifications, Everest shall promptly notify the JDC, and will provide any relevant materials to the JDC, for discussion at the next JDC meeting.

6.4 Manufacturing Reports. On [***] of each year following Everest's Manufacturing of the Compound or Licensed Products, Everest shall provide NPLH with a written report summarizing in sufficient detail for NPLH to verify Everest's compliance with its obligations under this Agreement, the API and drug product manufacturing processes being used by Everest, its Affiliates or Sublicensee, including product and manufacturing specifications, quality controls and assurances, test methods and raw material information.

6.5 Quality. The Parties agree that, following the Effective Date, they shall negotiate and enter into a separate Manufacturing Quality Agreement.

ARTICLE 7
COMMERCIALIZATION

7.1 General. Subject to the terms and conditions of this Agreement and the Commercialization Plan, Everest shall be responsible for all aspects of the Commercialization of the Licensed Products in the Licensed Field in the Territory, including: (a) developing and executing a commercial launch and pre-launch plan, (b) negotiating with applicable Government Authorities regarding the price and reimbursement status of the Licensed Products and obtaining and maintaining Pricing Approvals; (c) marketing, medical affairs, and promotion; (d) booking sales and distribution and performance of related services; (e) subject to the provisions of Section 5.5 (Recalls, Suspensions or Withdrawals) handling all aspects of order processing, invoicing and collection, inventory and receivables; (f) providing customer support, including handling medical queries, and performing other related functions; and (g) conforming its practices and procedures to Applicable Laws relating to the marketing, detailing and promotion of Licensed Products in the Licensed Field in the Territory. As between the Parties, Everest shall be solely responsible for the costs and expenses of Commercialization of the Licensed Products in the Licensed Field in the Territory.

7.2 Commercialization Plan. Everest shall conduct all Commercialization of Compounds and Licensed Products in the Licensed Field in the Territory in accordance with a comprehensive commercialization plan (as amended from time to time in accordance with this Agreement, the "**Commercialization Plan**"), the initial version of which Everest will prepare and provide to the JDC no later than [***] prior to the anticipated First Commercial Sale of Licensed Product in the Licensed Field in the Territory and which initial Commercialization Plan shall be subject to the review (but not approval) of the Parties through the JDC. From time to time, but at least once every Calendar Year, Everest will update the Commercialization Plan and submit such updated plan to the JDC for review and discussion. If any updated Commercialization Plan omits details that a NPLH representative reasonably believes is necessary for (i) the proper functioning of the JDC or (ii) to verify Everest's compliance with its obligations under this Agreement, then Everest shall take into reasonable consideration such comments and, if necessary, further update such Commercialize Plan. If the terms of the Commercialization Plan contradict, or create inconsistencies or ambiguities with, the terms of this Agreement, then the terms of this Agreement shall govern.

7.3 Commercial Diligence. Upon Regulatory Approval of a Licensed Product in a jurisdiction in the Territory, Everest, directly and/or with or through Affiliates or Sublicensees, shall use Commercially Reasonable Efforts to Commercialize such Licensed Product in the Licensed Field in such jurisdiction.

ARTICLE 8
FINANCIAL PROVISIONS

8.1 Upfront Payment. As partial consideration of the rights granted by NPLH to Everest hereunder, within [***] Business Days after the Effective Date, Everest shall pay to NPLH a one-time, non-refundable and non-creditable upfront payment of two million Dollars ($2,000,000).

8.2 Development and Regulatory Milestone Payments.

(a) As additional consideration of the rights granted by NPLH to Everest hereunder, within [***] calendar days after the first achievement of each milestone event below (a "**Milestone Event**") by or on behalf of Everest or any of its Affiliates or Sublicensees or by NPLH or any of its Affiliates or sublicensees, the Party achieving such Milestone Event or whose Affiliate or Sublicensee/sublicensee achieved such Milestone Event shall notify the other Party of the achievement of such Milestone Event. Milestone Events related to a Licensed Product trigger the corresponding milestone payment due to NPLH (a "**Milestone Payment**") and NPLH shall invoice Everest for the applicable non-refundable, non-creditable Milestone Payment corresponding to such Milestone Event as shown below, and Everest shall remit payment within [***] Business Days of the receipt of such invoice, as described in Section 8.6 (Currency; Exchange Rate; Payments).

Development and Regulatory Milestone Events for Licensed Products	**Milestone Payments (in U.S. Dollars)**
i.[***] ii.[***]	$[***]; or $[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]

[***]	$[***]
[***]	$[***]

(b) For clarity, if Everest does not timely make the written election in respect of the initial Milestone Event, then [***].

8.3 Commercial Milestones.

(a) Within [***] calendar days after the end of the first Fiscal Year in which aggregate annual Net Sales for that Fiscal Year for all Licensed Products reach any threshold indicated in the Milestone Events listed below, Everest shall notify NPLH of the achievement of such Milestone Event and NPLH shall invoice Everest for the corresponding non-refundable, non-creditable Milestone Payment set forth below and Everest shall remit payment to NPLH within [***] Business Days of the receipt of such invoice, as described in Section 8.6 (Currency; Exchange Rate; Payments).

Annual Net Sales Milestone Events	**Milestone Payments (in U.S. Dollars)**
First Fiscal Year in which aggregate annual Net Sales of Licensed Products in the Territory equal or exceed [***] U.S. dollars ($[***])	$[***]
First Fiscal Year in which aggregate annual Net Sales of Licensed Products in the Territory equal or exceed [***] U.S. dollars ($[***])	$[***]
First Fiscal Year in which aggregate annual Net Sales of Licensed Products in the Territory equal or exceed [***] U.S. dollars ($[***])	$[***]

(b) For the purposes of determining whether a Net Sales Milestone Event has been achieved, Net Sales of all Licensed Products in the Territory shall be aggregated. For clarity, the annual Net Sales Milestone Payments set forth in this Section 8.3 (Commercial Milestones) shall be payable only once for all Licensed Products, upon the first achievement of the applicable Milestone Event.

(c) If a Milestone Event in Section 8.3 (Commercial Milestones) is achieved and payment with respect to any previous Milestone Event has not been made, then such

previous Milestone Event shall be deemed achieved and Everest shall notify NPLH within [***] calendar days of such achievement. NPLH shall then invoice Everest for such unpaid previous Milestone Event(s) and Everest shall pay NPLH such unpaid previous milestone payment(s) within [***] Business Days of receipt of such invoice.

(d) Licensee shall provide NPLH with prompt written notice upon the occurrence of each Milestone Event set forth in Section 8.2 (Development and Regulatory Milestone Payments) and Section 8.3 (Commercial Milestones). In the event that, notwithstanding the fact that Everest has not given such a notice, NPLH believes any such Milestone Event has occurred, it shall so notify Everest in writing and shall provide to Everest data, documentation or other information that supports its belief. Any dispute under this Section 8.3(d) (Commercial Milestones - subsection (d)) that relates to whether or not a Milestone Event has occurred shall be referred to the JDC to be resolved in accordance with ARTICLE 3 (Governance) and shall be subject to resolution in accordance with Section 14.10 (Dispute Resolution). The Milestone Payments made for each Milestone Event shall be non-creditable and non-refundable.

8.4 Royalty Payments.

(a) **Royalty Rate**. In partial consideration of the rights granted by NPLH to Everest hereunder, Everest, its Affiliates and/or its or their respective Sublicensees, as applicable, shall pay to NPLH, on a jurisdiction-by-jurisdiction and Licensed Product-by-Licensed Product basis, non-refundable, non-creditable royalties based on the aggregate Net Sales of all Licensed Products sold by Everest, its Affiliates and/or its or their respective Sublicensees in the Territory during a Calendar Year at the rates set forth in the table below. The obligation to pay royalties will be imposed only once with respect to the same unit of a Licensed Product.

Calendar Year Net Sales (in Dollars) for all Licensed Products in the Territory	**Royalty Rates as a Percentage (%) of Net Sales**
Portion of Calendar Year Net Sales up to and including $[***]	[***]%
Portion of Calendar Year Net Sales that exceeds $[***], up to and including $[***]	[***]%
Portion of Calendar Year Net Sales that exceeds $[***]	[***]%

(b) **Royalty Term.** Royalties under this Section 8.4 (Royalty Payments) shall be payable on a jurisdiction-by-jurisdiction and Licensed Product-by-Licensed Product basis from the First Commercial Sale of a Licensed Product in a jurisdiction until the latest to occur of: (i) expiration of the last-to-expire Licensed Patent that contains a Valid Claim that would, but for

the licenses granted hereunder, be infringed by the Manufacture, use or sale of such Licensed Product (or the Compound contained in such Licensed Product) in such jurisdiction in the Territory; (ii) expiration of Regulatory Exclusivity for such Licensed Product in such jurisdiction in the Territory; and (iii) [***] years after the First Commercial Sale of the Licensed Product in such jurisdiction in the Territory (the "**Royalty Term**" for such Licensed Product and country).

(c) **Royalty Reports and Payment.** Within (i) [***] calendar days after each of the first [***] Calendar Quarters of each Spero Parent's fiscal years and (ii) [***] calendar days after the last Calendar Quarter of each of Spero Parent's fiscal years, in each case commencing with the Calendar Quarter during which the First Commercial Sale of any Licensed Product is made anywhere in the Territory, Everest shall provide NPLH with a report that contains the following information for the applicable Calendar Quarter, on a Licensed Product-by-Licensed Product and jurisdiction-by-jurisdiction basis: (A) Net Sales in the Territory; (B) a calculation of the royalty payment due on Net Sales in the Territory; and (C) the exchange rates used. Within [***] Business Days following the end of each such Calendar Quarter, Everest will pay NPLH all royalties owed with respect to Net Sales for such Calendar Quarter. If, during the following Calendar Quarter, Everest discovers that it reported an incorrect amount of Net Sales in the Territory and/or the amounts payment due on such Net Sales in the immediately preceding Calendar Quarter, then Everest may, subject to review by NPLH, adjust and reconcile any such calculation of Net Sales and/or any such underpayment or overpayment of royalty payments due, and shall timely report the same within [***] calendar days after such following Calendar Quarter.

8.5 Royalty Adjustments. Except as otherwise set forth in this Agreement, royalties due hereunder are subject to adjustment as set forth below (such adjustments to be prorated for the Calendar Quarter in which the adjustment becomes applicable):

(a) **Royalty Adjustment for Generic Competition.** In the event that in any jurisdiction in the Territory during the Royalty Term for a Licensed Product in a particular mode of administration there is Generic Competition for such Licensed Product in such mode of administration in such jurisdiction in any particular Calendar Quarter, then the royalty rate set forth in Section 8.4(a) (Royalty Rate) with respect to such Licensed Product in such jurisdiction in such Calendar Quarter shall be reduced by [***] percent ([***]%); provided that in no event shall any royalty payment payable to NPLH for any Licensed Product in a jurisdiction in a given Calendar Quarter be reduced as a result of the payment reduction set forth in this subsection (b) of this Section 8.5 (Royalty Adjustments), in the aggregate, to less than [***] percent ([***]%) of the amount otherwise payable to the NPLH with respect to such Licensed Product in such jurisdiction in such Calendar Quarter in accordance with Section 8.4 (Royalty Payments); and

(b) **Unit Sales**. Unit sales shall be measured by IQVIA (or, in the absence of such data, an appropriate end user-level database mutually agreed by the Parties).

8.6 Currency; Exchange Rate; Payments. All payments required to be made by Everest under this Agreement shall be made in Dollars and shall be paid directly by Everest and not any of its Affiliates. All payments payable to, or invoiced from or on behalf of, NPLH shall be paid bank wire transfer in immediately available funds to one or more bank accounts of

NPLH (or behalf of NPLH to a bank account of Spero Parent), as designated in written notice from NPLH. If any currency conversion shall be required in connection with any payment hereunder, such conversion shall be made by using the exchange rates at the closing on the last Business Day of the Calendar Quarter to which such payment relates as reported in The Wall Street Journal on the following day.

8.7 Late Payments. Any payments or portions thereof due hereunder that are not paid on the date such payments are due under this Agreement shall bear interest at an annual rate equal to [***] percentage points above the prime rate as published by *The Wall Street Journal* or any successor thereto on the first day of each Calendar Quarter in which such payments are overdue calculated on the number of days such payment is delinquent.

8.8 Taxes.

(a) **Taxes on Income.** Notwithstanding anything else set forth in this Section 8.8 (Taxes), each Party shall solely bear and pay all Taxes imposed on such Party's net income or gain (however denominated) arising directly or indirectly from the activities of the Parties under this Agreement.

(b) **Tax Payments.** The upfront payment, milestone payments, royalties, Sublicensing Revenue payments and any other payment payable by Everest to NPLH pursuant to this Agreement (each, a "**Payment"**) shall be paid free and clear of any and all taxes (which, for clarity, shall be the responsibility of Everest), except for any withholding taxes required by Applicable Laws. Except as provided in this Section 8.8, Everest shall be solely responsible for paying any and all taxes (other than withholding taxes required by Applicable Laws to be deducted from Payments and remitted by Everest) levied on account of, or measured in whole or in part by reference to, any Payments it makes. Everest shall deduct or withhold from the Payments any taxes that it is required by Applicable Laws to deduct or withhold. Notwithstanding the foregoing, if NPLH is entitled under any applicable tax treaty to a reduction of rate of, or the elimination of, applicable withholding tax, it may deliver to Everest or the appropriate governmental authority (with the assistance of Everest to the extent that this is reasonably required and is requested in writing) the prescribed forms necessary to reduce the applicable rate of withholding or to relieve Everest of its obligation to withhold such tax and Everest shall apply the reduced rate of withholding or dispense with withholding, as the case may be; provided that NPLH has received evidence of Everest's delivery of all applicable forms (and, if necessary, its receipt of appropriate governmental authorization) at least [***] Business Days prior to the time that the such Payment is due. If, in accordance with the foregoing, Everest withholds any amount, it shall pay to NPLH the balance when due, make timely payment to the proper taxing authority of the withheld amount and send to NPLH proof of such payment to such taxing authority within [***] Business Days following such payment.

(c) **Transfer Tax**. Subject to Sections 8.8(a) (Taxes on Income) and 8.8(b) (Tax Payments) above, Everest and NPLH shall each bear and pay [***] percent ([***]%) of any transfer, stamp, value added, sales, use, or similar Taxes or obligations imposed on amounts payable by Everest to NPLH ("**Transfer Tax**") in connection with this Agreement. All Payments are exclusive of Transfer Taxes. If any Transfer Tax is chargeable in respect of any

Payments, Everest shall pay [***] percent ([***]%) of such Transfer Tax at the applicable rate in respect of any such Payments following the receipt of a Transfer Tax invoice in the appropriate form issued by NPLH in respect of those Payments, such Transfer Taxes to be payable on the later of the due date of the payment of the Payments to which such Transfer Tax relates and [***] Business Days after the receipt by Everest of the applicable invoice relating to that Transfer Tax payment.

8.9 Financial Records and Audit. Everest shall (and shall ensure that its Affiliates and Sublicensees will) maintain complete and accurate books and records pertaining to the Commercialization of Licensed Products hereunder, including books and records of invoiced sales and Net Sales of Licensed Products, in sufficient detail to calculate and verify all amounts payable hereunder and in sufficient detail to permit NPLH to confirm the accuracy of any royalty payments, Sublicensing Revenue and other amounts paid or payable under this Agreement and to verify the achievement of Milestone Events under this Agreement. Everest shall and shall cause its Affiliates and its and their Sublicensees to, retain such books and records until the later of (a) [***] years after the end of the period to which such books and records pertain; (b) the expiration of the applicable tax statute of limitations (or any extensions thereof); and (c) for such period as may be required by Applicable Laws. Upon at least [***] Business Days' prior notice, such records shall be open for examination, during regular business hours, for a period of [***] Calendar Years from the end of the Calendar Year to which such records pertain, and not more often than once each Fiscal Year, by an independent certified public accountant selected by NPLH and reasonably acceptable to Everest, for the sole purpose of verifying for NPLH the accuracy of the financial reports furnished by Everest under this Agreement or of any payments made, or required to be made, by Everest to NPLH pursuant to this Agreement. The independent public accountant shall disclose to NPLH only (x) the accuracy of Net Sales reported and the basis for royalty, Sublicensing Revenue, Milestone Payments and any other payments made to NPLH under this Agreement and (y) the difference, if any, by which such reported and paid amounts vary from amounts determined as a result of the Audit and the details concerning such difference. Except as required by Applicable Laws, no other information shall be provided to NPLH. No record may be audited more than once. NPLH shall bear the full cost of such audit unless such audit reveals an underpayment by Everest of more than [***] percent ([***]%) of the amount actually due for any Calendar Year being audited, in which case Everest shall reimburse NPLH for the reasonable costs and expenses for such audit. Unless disputed pursuant to Section 8.10 (Audit Dispute), Everest shall pay to NPLH any underpayment discovered by such audit within [***] Business Days after the accountant's report, plus interest (as set forth in Section 8.7 (Late Payments)) from the original due date. If the audit reveals an overpayment by Everest, then Everest may take a credit for such overpayment against any future payments due to NPLH.

8.10 Audit Dispute. If Everest disputes the results of any audit conducted pursuant to Section 8.9 (Financial Records and Audit), the Parties shall work in good faith to resolve the disagreement. If the Parties are unable to reach a mutually acceptable resolution of any such dispute within [***] Business Days, the dispute shall be submitted for resolution to a certified public accounting firm jointly selected by each Party's certified public accountants or to such other Person as the Parties shall mutually agree (the "**Auditor**"). The decision of the Auditor shall be final and the costs of such procedure as well as the initial audit shall be borne between

the Parties in such manner as the Auditor shall determine. If the Auditor determines that there has been an underpayment by Everest, Everest shall pay to NPLH the underpayment within [***] Business Days after the Auditor's decision, plus interest (as set forth in Section 8.7 (Late Payments)) from the original due date. If the Auditor determines that there has been an overpayment by Everest, then Everest may take a credit for such overpayment against any future payments due to NPLH.

ARTICLE 9
INTELLECTUAL PROPERTY RIGHTS

9.1 Ownership of Intellectual Property

(a) **Ownership of Technology**. As between the Parties:

(1) NPLH shall solely own on a worldwide basis all right, title and interest in and to any and all NPLH Sole Inventions, whether or not patented or patentable, and any and all NPLH Sole Invention Patents; and

(2) Everest shall solely own on a worldwide basis all right, title and interest in and to any and all Everest Sole Inventions, whether or not patented or patentable, and any and all Everest Sole Invention Patents.

For clarity, each Party shall own on a worldwide basis and retain all right, title and interest in and to any and all Know-How, Inventions, Patents and other intellectual property rights that are owned or otherwise Controlled (other than pursuant to the license grants set forth in Section 2.1 (Licenses to Everest) and 2.2 (License to NPLH)) by such Party or its Affiliates or its or their (sub)licensees (or Sublicensees) (as applicable) outside of this Agreement.

(b) **Ownership of Joint Patents and Joint Inventions**. As between the Parties:

(1) Each of NPLH and Everest shall own an equal, undivided interest in any and all Joint Inventions and Joint Invention Patents; and

(2) Each of NPLH and Everest shall promptly disclose to the other in writing, and shall cause its Affiliates and its and their respective Sublicensees to so disclose, the development, making, conception or reduction to practice of any Joint Inventions. Subject to the licenses granted under Section 2.1 (License to Everest) and Section 2.2 (License to NPLH), each of NPLH and Everest shall have the right to Exploit the Joint Inventions and Joint Invention Patents.

(c) **United States Law**. The determination of whether Inventions, Know-How and other intellectual property rights are conceived, discovered, developed or otherwise made by a Party for the purpose of allocating proprietary rights (including Patent, copyright or other intellectual property rights) therein, shall, for purposes of this Agreement, be made in accordance with Applicable Laws in the United States as such law exists as of the Effective Date irrespective of where or when such conception, discovery, development or making occurs;

provided that if the application of such United States Applicable Laws prevents or materially impairs the proper prosecution or maintenance of Patent Rights in any jurisdiction in the Territory, then the Parties shall mutually agree to the application of an appropriate Applicable Laws in order to best advance and maintain the prosecution and maintenance of such Patents in such jurisdiction in the Territory. Each of NPLH and Everest shall, and does hereby, assign, and shall cause its Affiliates and its and their (sub)licensees and Sublicensees to so assign, to the other Party, without additional compensation, such right, title and interest in and to any Inventions, Know-How, Patents and other intellectual property rights with respect thereto, as is necessary to fully effect, as applicable, the sole or joint ownership as provided for in Section 9.1(a) (Ownership of Technology) or 9.1(b) (Ownership of Joint Patents and Joint Inventions).

(d) **Assignment Obligation**. Each Party shall cause all Persons who perform Development activities, Manufacturing activities or regulatory activities for such Party under this Agreement or who conceive, discover, develop or otherwise make any Inventions, Know-How or other intellectual property rights by or on behalf of either Party or its Affiliates or its or their (sub)licensees (or Sublicensees) under or in connection with this Agreement to be under an obligation to assign to such Party their rights in any Inventions, Know-How, Patents and other intellectual property, except where Applicable Laws requires otherwise and except in the case of governmental, not-for-profit and public institutions that have standard policies against such an assignment (in which case, a suitable license or right to obtain such a license, shall be obtained).

(e) **Ownership of Product Trademarks.** Subject to Section 11.3 (Effect of Termination) and Section 5.3(d) (Discontinuation), as between the Parties, (i) Everest shall own all right, title and interest in and to the Product Trademarks in the Territory, (ii) Everest shall have the right to market the Licensed Products in the Licensed Field in the Territory under the Product Trademarks and all goodwill associated therewith will inure to the benefit of Everest and (iii) NPLH may not use the Product Trademarks without obtaining a proper trademark license from Everest (except to the extent necessary to perform its obligations under this Agreement).

(f) **Ownership of Corporate Names**. As between the Parties, NPLH and/or Spero Parent shall retain all right, title and interest in and to its Corporate Names.

(g) **Ownership of Development Data**. Subject to ARTICLE 2 (Licenses), Section 5.3(d) (Discontinuation) and Section 11.3 (Effect of Termination), Everest shall own Everest Development Data and NPLH shall own NPLH Development Data.

9.2 Patent Prosecution and Maintenance.

(a) NPLH shall have the first right, but not the obligation, to control the preparation, filing, prosecution (including any interferences, reissue proceedings and reexaminations) and maintenance of all Licensed Patents, Joint Patents and Everest Patents, both in and outside the Territory, by counsel of its own choice, except that such counsel in the Territory shall be reasonably acceptable to Everest (such acceptance not to be unreasonably withheld, delayed or conditioned). NPLH shall consult with Everest and keep Everest reasonably informed of the status of such Patents in the Territory and shall promptly provide Everest with all material correspondence received from any patent authority in the Territory in

connection therewith. In addition, NPLH shall promptly provide Everest with drafts of all proposed material filings and correspondence to any patent authority in the Territory with respect to such Patents for Everest's review and comment prior to the submission of such proposed filings and correspondence. NPLH shall confer with Everest and consider in good faith Everest's comments prior to submitting such filings and correspondence, provided that Everest provides such comments within [***] Business Days (or a shorter period reasonably designated by NPLH if [***] Business Days is not practicable given the filing deadline) of receiving the draft filings and correspondence from NPLH. The costs and expenses of such preparation, filing, prosecution and maintenance of the Licensed Patents, Joint Patents and Everest Patents shall be shared by NPLH and Everest such that NPLH shall be responsible for the costs and expenses of such preparation, filing, prosecution and maintenance of the Licensed Patents, Joint Patents and Everest Patents outside the Territory and Everest shall be responsible for the costs and expenses of such preparation, filing, prosecution and maintenance of the Licensed Patents, Joint Patents and Everest Patents in the Territory. For the avoidance of doubt, NPLH shall be responsible for all costs incurred prior to the Effective Date with respect to the prosecution and maintenance of any Licensed Patents. If Everest reasonably determines that a Licensed Patent added after the Effective Date (other than Patent Rights added by an In-License Agreement that Everest has accepted pursuant to Section 2.4(b)(1) (In-License Agreements)) or Joint Patent that Everest subsequently determines is of low value to Everest, then Everest has the right upon at least [***] days' prior notice to remove such Licensed Patent or Joint Patent from the Licensed Technology hereunder, in which case, following delivery of such notice to NPLH, (1) the license of Licensed Technology to Everest under Section 2.1 (License to Everest) as to such Licensed Patent or Joint Patent shall be terminated; (2) Everest shall no longer be obligated to pay for any costs and expenses of preparation, filing, prosecution and maintenance of such Licensed Patent or Joint Patent, as the case may be; and (3) if requested by NPLH, Everest shall assign, and shall cause its Affiliates and its and their (sub)licensees and Sublicensees to so assign, to NPLH, without additional compensation, Everest's right, title and interest in and to the relevant Joint Patent.

(b) Subject to the provisions of Section 5.3(d) (Discontinuation), in the event that NPLH desires to abandon or cease prosecution or maintenance of any Licensed Patent, Joint Patent or Everest Patent in the Territory (or any jurisdiction therein), NPLH shall provide reasonable prior written notice to Everest of such intention to abandon (which notice shall, to the extent possible, be given no later than [***] Business Days prior to the next deadline for any action that must be taken with respect to any such Patent in the relevant patent office in the Territory or such jurisdiction). In such case, upon Everest's written election provided no later than [***] Business Days after such notice from NPLH, Everest shall have the right to assume prosecution and maintenance of such Licensed Patent, Joint Patent or Everest Patent at Everest's sole cost and expense. If Everest does not provide such election within [***] Business Days after such notice from NPLH, NPLH may, in its sole discretion, continue prosecution and maintenance of such Patent in the Territory (or the relevant jurisdiction), at Everest's costs and expense, or discontinue prosecution and maintenance of such Patent in the Territory (or the relevant jurisdiction).

9.3 Cooperation of the Parties. Each Party agrees to cooperate fully in the preparation, filing, prosecution and maintenance of Patents under Section 9.2 (Patent Prosecution and Maintenance), at its own cost. Such cooperation includes: (a) executing all papers and

instruments, or requiring its employees or contractors, to execute such papers and instruments, so as enable the applicable Party to apply for and to prosecute patent applications in any country as permitted by Section 9.2 (Patent Prosecution and Maintenance); and (b) promptly informing the other Party of any matters coming to such Party's attention that may affect the preparation, filing, prosecution or maintenance of any such patent applications.

9.4 Infringement by Third Parties.

(a) **Notice.** In the event that either NPLH or Everest becomes aware of any infringement or threatened infringement by a Third Party of any Licensed Patent or Joint Patent in and/or outside the Territory, which infringing activity involves the using, making, importing, offering for sale or selling of a Licensed Product (regardless of whether or not Everest and/or NPLH is currently Developing using, making, importing, offering for sale, selling, or otherwise Commercializing the same Licensed Product), or the submission to a Party or a Regulatory Authority in and/or outside the Territory of an application for a product referencing a Licensed Product, or any declaratory judgment or equivalent action challenging any Licensed Patent or Joint Patent in and/or inside the Territory in connection with any such infringement (each, a "**Product Infringement**"), it will promptly notify the other Party in writing to that effect. Any such notice shall include evidence to support an allegation of infringement or threatened infringement, or declaratory judgment or equivalent action, by such Third Party.

(b) **Enforcement of Licensed Patents and Joint Patents**

(1) If such Product Infringement is occurring solely in the Territory and not outside the Territory, Everest shall have the first right, as between NPLH and Everest, but not the obligation, to bring an appropriate suit or take other action against any Person or entity engaged in, or to defend against, a Product Infringement in the Territory of any Licensed Patent or Joint Patent, at its own expense and by counsel of its own choice. NPLH shall have the right, at its own expense, to be represented in any such action by counsel of its own choice, and Everest and its counsel will reasonably cooperate with NPLH and its counsel in strategizing, preparing and prosecuting any such action or proceeding. If Everest fails to bring an action or proceeding with respect to such Product Infringement in the Territory of any Licensed Patent or Joint Patent within (A) [***] Business Days following the notice of alleged infringement or declaratory judgment or (B) [***] Business Days before the time limit, if any, set forth in the Applicable Laws for the filing of such actions, whichever comes first, NPLH shall have the right, but not the obligation, to bring and control any such action at its own expense and by counsel of its own choice, and Everest shall have the right, at its own expense, to be represented in any such action by counsel of its own choice. Except as otherwise agreed by the Parties as part of a cost-sharing arrangement, any recovery or damages realized as a result of such action or proceeding with respect to Product Infringement of any Licensed Patent or Joint Patent, or settlement of the same, shall be used (A) first, to reimburse the Parties' documented out-of-pocket legal expenses relating to the action or proceeding; and (B) any remainder after such reimbursement is made shall be shared by Everest and NPLH, in proportion to (1) Everest's loss of sales or profits with respect to a Licensed Product in the Licensed Field in the Territory and (2) NPLH's lost Milestone Payments and royalty payments that would otherwise be payable to NPLH in the absence of such Product Infringement in the Territory, provided, that to the extent that any award

or settlement (whether by judgment or otherwise) with respect to any Licensed Patent or Joint Patent is attributable to loss of sales or profits with respect to a Licensed Product in the Licensed Field in the Territory, any amounts (except punitive damages) that may be recovered or realized by Everest shall be considered Net Sales and subject to the royalty obligations under Section 8.4 (Royalty Payments) and the commercial Milestone Payment obligations under Section 8.3 (Commercial Milestones).

(2) If such Product Infringement is occurring both in and outside the Territory, NPLH shall have the first right, as between NPLH and Everest, but not the obligation, to bring an appropriate suit or take other action against any Person or entity engaged in, or to defend against, such Product Infringement (including in the Territory) of any Licensed Patent or Joint Patent, at its own expense and by counsel of its own choice. Everest shall have the right, at its own expense, to be represented in any such action solely in the Territory by counsel of its own choice, and Everest and its counsel will reasonably cooperate with NPLH and its counsel in strategizing, preparing and prosecuting any such action or proceeding. If NPLH fails to bring an action or proceeding in the Territory with respect to such Product Infringement of any Licensed Patent or Joint Patent within (A) [***] Business Days following the notice of alleged infringement or declaratory judgment or (B) [***] Business Days before the time limit, if any, set forth in the Applicable Laws for the filing of such actions, whichever comes first, Everest shall have the right, but not the obligation, to bring and control any such action in the Territory at its own expense and by counsel of its own choice, and NPLH shall have the right, at its own expense, to be represented in any such action by counsel of its own choice. Except as otherwise agreed by the Parties as part of a cost-sharing arrangement, any recovery or damages realized as a result of such action or proceeding with respect to Product Infringement of any Licensed Patent or Joint Patent, or settlement of the same, shall be used (A) first, to reimburse the Parties' documented out-of-pocket legal expenses relating to the action or proceeding; and (B) any remainder after such reimbursement is made shall be shared by Everest and NPLH, in proportion to (1) Everest's loss of sales or profits with respect to a Licensed Product in the Licensed Field in the Territory and (2) NPLH's loss of sales or profits with respect to a Licensed Product in the Licensed Field outside the Territory; provided, that to the extent that any award or settlement (whether by judgment or otherwise) is allocated to Everest, any such amounts (except punitive damages) so allocated to Everest shall be considered Net Sales and subject to the royalty obligations under Section 8.4 (Royalty Payments) and the commercial Milestone Payment obligations under Section 8.3 (Commercial Milestones).

(c) **Cooperation.** In the event a Party brings an action in accordance with this Section 9.4 (Infringement by Third Parties), the other Party shall cooperate fully, including, if required to bring such action, the furnishing of a power of attorney or being named as a party to such action.

(d) **Other Infringement**. NPLH shall have the sole right, but not the obligation, to bring and control, at its own cost and expense, any legal action in connection with any Product Infringement of any Licensed Patent or Joint Patent outside the Territory and any legal action in connection with any infringement of any Joint Patent outside the Territory that is not a Product Infringement. Everest shall have the sole right, but not the obligation, to bring and control, at its own cost and expense, any legal action in connection with any infringement of any

Joint Patent in the Territory that is not a Product Infringement. Any recovery or damages realized as a result of such action or proceeding with respect to Product Infringement of any Licensed Patent or Joint Patent shall be used (A) first, but only if a Joint Patent was the subject of such legal action, to reimburse the Parties' documented out-of-pocket legal expenses relating to such action or proceeding; and (B) any remainder after such reimbursement, if applicable, shall be retained by the Party initiating such action or proceeding.

9.5 Infringement Claims by Third Parties. If the Exploitation of a Licensed Product in the Licensed Field in the Territory pursuant to this Agreement results in, or is reasonably expected to result in, any claim, suit or proceeding by a Third Party against Everest or any of its Affiliates or Sublicensees alleging infringement by Everest or any of its Affiliates or its or their Sublicensees, distributors or customers (a "**Third Party Infringement Claim**"), including any defense or counterclaim in connection with a Product Infringement action initiated pursuant to Section 9.4(b) (Enforcement of Licensed Patents and Joint Patents), the Party first becoming aware of such alleged infringement shall promptly notify the other Party thereof in writing. As between the Parties, subject to ARTICLE 13 (Indemnification; Liability): (a) Everest shall be responsible for defending any such claim, suit or proceeding at its sole cost and expense, using counsel of Everest's choice; (b) NPLH may participate in any such claim, suit or proceeding with counsel of its choice at its sole cost and expense; provided that Everest shall retain the right to control such claim, suit or proceeding; (c) NPLH shall, and shall cause its Affiliates to, assist and co-operate with Everest, as Everest may reasonably request from time to time, in connection with its activities set forth in this Section 9.5 (Infringement Claims by Third Parties), including where necessary, furnishing a power of attorney solely for such purpose or joining in, or being named as a necessary party to, such action, providing access to relevant documents and other evidence and making its employees available at reasonable business hours; provided that Everest shall reimburse NPLH for its reasonable and verifiable out-of-pocket costs and expenses incurred in connection therewith; (d) Everest shall keep NPLH reasonably informed of all material developments in connection with any such claim, suit or proceeding; (e) Everest agrees to provide NPLH with copies of all material pleadings filed in such action and to allow NPLH reasonable opportunity to participate in the defense of the Claims; and (f) any damages, or awards, including royalties, incurred or awarded in connection with any Third Party Infringement Claim defended under this Section 9.5 (Infringement Claims by Third Parties) shall be borne by Everest subject to ARTICLE 13 (Indemnification; Liability).

9.6 Invalidity or Unenforceability Defenses or Actions. Each Party shall promptly notify the other Party in writing of any alleged or threatened assertion of invalidity or unenforceability of any of the Licensed Patents, Joint Patents or Everest Patents worldwide, by a Third Party and of which such Party becomes aware. As between the Parties: (a) NPLH and Everest shall coordinate with each other to defend and control the defense of the validity and enforceability of any Joint Patents that claim the composition of matter of the Licensed Compound and Licensed Products in the Territory and share the cost and expense thereof; (b) NPLH shall have the first right, but not the obligation, to defend and control the defense of the validity and enforceability of any Licensed Patents in the Territory or Joint Patents outside the Territory, at its sole cost and expense, using counsel of NPLH's choice; and (c) Everest shall have the first right, but not the obligation, to defend and control the defense of the validity and enforceability of the Everest Patents worldwide or Joint Patents in the Territory at its sole cost

and expense, using counsel of Everest's choice. Notwithstanding anything to the contrary above, Everest shall have the first right, but not the obligation, to defend and control the defense of the validity and enforceability of the Licensed Patents in the Territory at its sole cost and expense, using counsel of Everest's choice, when such invalidity or unenforceability is raised as a defense or counterclaim in connection with an Infringement action initiated by Everest pursuant to Section 9.4(b) (Enforcement of Licensed Patents and Joint Patents). For purposes of this Section 9.6 (Invalidity or Unenforceability Defenses or Actions), the Party defending and controlling the defense of the validity and enforceability pursuant to the foregoing sentence with respect to a Patent shall be the "**Controlling Party**". With respect to any such claim, suit or proceeding in the Territory under this Section 9.6 (Invalidity or Unenforceability Defenses or Actions), the non-Controlling Party may participate in such claim, suit or proceeding with counsel of its choice at its sole cost and expense; provided that the Controlling Party shall retain control of the defense in such claim, suit or proceeding. If the Controlling Party elects not to defend the applicable Patents in a suit, then the Controlling Party shall notify the non-Controlling Party of such election at [***] Business Days before the time limit, if any, set forth in Applicable Laws for defending such actions, and the non-Controlling Party may assume control of the defense of any such claim, suit or proceeding at its sole cost and expense. The non-Controlling Party in such an action shall, and shall cause its Affiliates to, assist and co-operate with the Controlling Party, as such Controlling Party may reasonably request from time to time. in connection with its activities set forth in this Section 9.6 (Invalidity or Unenforceability Defenses or Actions), including where necessary, furnishing a power of attorney solely for such purpose or joining in, or being named as a necessary party to, such action, providing access to relevant documents and other evidence and making its employees available at reasonable business hours; provided that the Controlling Party shall reimburse the non-Controlling Party for its reasonable and verifiable out-of-pocket costs and expenses incurred in connection therewith. In connection with any activities with respect to a defense, claim or counterclaim relating to the Licensed Patents, Everest Patents or Joint Patents licensed under Section 2.1 (License to Everest) or Section 2.2 (License to NPLH), the Controlling Party shall (i) consult with the non-Controlling Party as to the strategy for such activities, (ii) consider in good faith any comments from the non-Controlling Party and (iii) keep the non-Controlling Party reasonably informed of any material steps taken and provide copies of all material documents filed, in connection with such defense, claim or counterclaim.

9.7 Consent for Settlement. Neither Party shall unilaterally enter into any settlement or compromise of any action or proceeding under this ARTICLE 9 (Intellectual Property Rights) that would in any manner alter, diminish, or be in derogation of the other Party's rights under this Agreement or otherwise without the prior written consent of such other Party, which shall not be unreasonably withheld, conditioned or delayed.

9.8 Common Ownership under Joint Research Agreement. Notwithstanding anything to the contrary in this ARTICLE 9, no Party shall have the right to make an election under 35 U.S.C. 102(c) when exercising its rights under this ARTICLE 9 without the prior written consent of the other Party. With respect to any such permitted election, the Parties shall co-ordinate their activities with respect to any submissions, filings or other activities in support thereof. The Parties acknowledge and agree that this Agreement is a "joint research agreement" as defined in 35 U.S.C. 100(h).

9.9 Patent Extensions. NPLH and Everest shall jointly, following consultation with each other, have decision making authority regarding, and they shall cooperate with each other, in obtaining, patent term restoration, supplemental protection certificates or their equivalents, and patent term extensions with respect to the Licensed Patents, Joint Patents, and Everest Patents in the Territory where applicable. If mutually agreed, Everest shall file for such extensions at the Parties' shared cost and expe nse. If the Parties cannot agree, the matter will be referred to the JDC for decision pursuant to Section 3.3 (JDC Decision Making).

9.10 Trademarks. NPLH and Everest shall provide to the other Party prompt written notice of any actual or threatened infringement of the Product Trademarks or Spero Trademarks in the Territory and of any actual or threatened Claim that the use of the Product Trademarks or Spero Trademarks in the Territory violates the rights of any Third Party, in each case, of which such Party becomes aware. Everest shall own and be responsible, at its expense, for all Product Trademarks, trade names, branding or logos related to the Compound or Licensed Products in the Licensed Field in the Territory. Everest shall have the sole right to take such action as Everest deems necessary against a Third Party based on any alleged, threatened or actual infringement, dilution, misappropriation or other violation of or unfair trade practices or any other like offense relating to, the Product Trademarks by a Third Party in the Territory at its sole cost and expense and using counsel of its own choice and Everest shall retain any damages or other amounts collected in connection therewith.

9.11 Spero Trademarks. If Everest is lawfully required by any Regulatory Authority to use any of the Spero Trademarks or any other Trademark used by NPLH to market, promote, distribute and/or sell any Licensed Product in the Licensed Field outside the Territory for the purpose of Commercialization of the relevant Licensed Product in a jurisdiction in the Territory, Everest shall promptly notify NPLH, and NPLH or Spero Parent, as the case may be, shall immediately grant Everest a non-exclusive, fully-paid, royalty-free and sublicensable license to use such Spero Trademark or such other Trademark solely in connection with the Commercialization of the relevant Licensed Product in the Licensed Field in such jurisdiction in the Territory; provided that any such license shall automatically terminate on the early to occur of (i) the expiration or termination of this Agreement; (ii) the abandonment by Everest of such Licensed Product in such jurisdiction; and (iii) the abandonment by Everest of such Licensed Product in the Territory. Except as provided for in the previous clause, if Everest wishes to obtain a license under Spero Trademarks to use such Spero Trademarks with respect to the Commercialization of the Licensed Products in the Licensed Field in the Territory, Everest shall notify Spero thereof and the Parties shall negotiate a license with respect thereto, with license terms consistent with this Agreement.

ARTICLE 10
CONFIDENTIALITY; PUBLICATION

10.1 Duty of Confidence. Subject to the other provisions of this ARTICLE 10 (Confidentiality; Publication):

(a) all Confidential Information disclosed by a Party (the "**Disclosing Party**") or its Affiliates under this Agreement will be maintained in confidence and otherwise

safeguarded by the recipient Party (the "**Receiving Party**") and its Affiliates using at least the same standard of care as the Receiving Party uses to protect its own proprietary or Confidential Information (but in no event less than reasonable care);

(b) the Receiving Party, its Affiliates and Representatives may only use any such Confidential Information for the purposes of performing its obligations or exercising its rights under this Agreement; and

(c) the Receiving Party may disclose Confidential Information of the Disclosing Party only to: (i) the Receiving Party's Affiliates; and (ii) employees, directors, agents, contractors, Subcontractors, consultants and advisers of the Receiving Party and its Affiliates and, in the case of Everest as the Receiving Party, its Sublicensees, in each case to the extent reasonably necessary for the purposes of, and for those matters undertaken pursuant to, this Agreement (collectively, the "**Representatives**"); provided, that such Representatives are bound to maintain the confidentiality, and not to make any unauthorized use, of the Confidential Information in a manner consistent with this ARTICLE 10 (Confidentiality; Publication).

10.2 Exceptions. The foregoing obligations as to particular Confidential Information of a Disclosing Party shall not apply to the extent that the Receiving Party can demonstrate by competent evidence that such Confidential Information:

(a) is known by the Receiving Party at the time of its receipt, and not through a prior disclosure by the Disclosing Party, as demonstrated by documentation or other competent proof of the Receiving Party, but excluding Joint Inventions or the terms of this Agreement;

(b) is in the public domain by use and/or publication before its receipt from the Disclosing Party, or thereafter enters the public domain through no fault of, or breach of this Agreement by, the Receiving Party;

(c) is subsequently disclosed to the Receiving Party on a non-confidential basis by a Third Party who, to the Receiving Party's knowledge after reasonable inquiry, may lawfully do so and is not under an obligation of confidentiality to the Disclosing Party; or

(d) is developed by the Receiving Party independently and without use of or reference to any Confidential Information disclosed to, or materials provided to, it by or on behalf of the Disclosing Party, as shown by contemporaneous written documents of the Receiving Party.

10.3 Authorized Disclosures. Notwithstanding the obligations set forth in Section 10.1 (Duty of Confidence), the Receiving Party may disclose Confidential Information of the Disclosing Party and the terms of this Agreement to the extent such disclosure is reasonably necessary for such Disclosing Party to perform its obligations or exercise its rights under this Agreement, in the following instances:

(a) filing or prosecuting of Patents as permitted by this Agreement;

(b) enforcing the Receiving Party's rights under this Agreement or performing the Receiving Party's obligations under this Agreement;

(c) in Regulatory Filings for Licensed Products that such Party has the right to file under this Agreement;

(d) prosecuting or defending litigation as permitted by this Agreement;

(e) to the Receiving Party's Representatives and actual or potential Sublicensees (in the case of Everest), in each case, who have a need to know such Confidential Information in order for the Receiving Party to exercise its rights or fulfill its obligations under this Agreement; provided, in each case, that any such Person agrees to be bound by terms of confidentiality and non-use (or, in the case of the Receiving Party's attorneys and independent accountants, such Person is obligated by applicable professional or ethical obligations) at least as restrictive as those set forth in this ARTICLE 10 (Confidentiality; Publication);

(f) to actual or potential investors, investment bankers, lenders, other financing sources or acquirers (and attorneys and independent accountants thereof) in connection with potential investment, acquisition, collaboration, merger, public offering, due diligence or similar investigations by such Third Parties or in confidential financing documents; provided, in each case, that any such Third Party agrees to be bound by terms of confidentiality and non-use (or, in the case of the Receiving Party's attorneys and independent accountants, such Third Party is obligated by applicable professional or ethical obligations) that are no less stringent than those contained in this Agreement (except to the extent that a shorter confidentiality period is customary in the industry); and

(g) such disclosure is required by court order, judicial or administrative process or Applicable Laws; provided that in such event the Receiving Party shall promptly inform the Disclosing Party of such required disclosure and provide the Disclosing Party an opportunity to challenge or limit the disclosure obligations. Confidential Information that is disclosed as required by court order, judicial or administrative process or Applicable Laws shall remain otherwise subject to the confidentiality and non-use provisions of this ARTICLE 10 (Confidentiality; Publication), and the Receiving Party shall take all steps reasonably necessary, including seeking of confidential treatment or a protective order, to ensure the continued confidential treatment of such Confidential Information.

10.4 Publication. Prior to publishing or presenting the results of any studies carried out under this Agreement, Everest shall submit the draft of the publication or presentation to NPLH no later than [***] Business Days prior to the planned submission for publication or presentation for NPLH's comment. Everest shall: (a) consider in good faith any comments thereto provided by NPLH within such [***] day period; and (b) remove any Confidential Information of NPLH if requested by NPLH. NPLH shall be deemed to have consented to such publication or presentation if it has not sent any response to Everest's request within [***] Business Days of receipt of the request by Everest by written notice to NPLH delivered pursuant to Section 14.9. NPLH may reasonably request a reasonable delay in publication or presentation in order to protect patentable information. If NPLH reasonably requests a delay, then Everest

shall, and shall ensure that its Affiliate(s) or the Sublicensee(s) shall, delay submission or presentation for a period of [***] Business Days (or such shorter period as may be mutually agreed by the Parties) to enable NPLH to file patent applications protecting NPLH's rights in such information.

10.5 Publicity/Use of Names. The Parties intend to agree upon the content of one (1) or more press releases, the release of which the Parties shall coordinate in order to accomplish such release promptly upon execution of this Agreement. Other than as set forth in the prior sentence, no other disclosure of the existence, or the terms, of this Agreement may be made by either Party or its Affiliates, and neither Party shall use the name, trademark, trade name or logo of the other Party, its Affiliates or their respective employee(s) in any publicity, promotion, news release or disclosure relating to this Agreement or its subject matter, without the prior express written permission of the other Party, except as may be required by Applicable Laws. Notwithstanding the above, each Party and its Affiliates may disclose on its website, in news releases, its promotional materials and other disclosures relating to this Agreement that the other Party is a development partner of such Party for the Licensed Products in the Territory and may use the other Party's name and logo in conjunction with such disclosure. Notwithstanding the foregoing:

(a) A Party may disclose this Agreement and its terms, and material developments or material information generated under this Agreement, in news releases and securities filings with the U.S. Securities and Exchange Commission ("**SEC**") (or equivalent foreign agency) to the extent required by Applicable Laws after complying with the procedure set forth in this Section 10.5 (Publicity/Use of Names). In such event, the Party seeking to make such disclosure will prepare a draft of such disclosure together with, if applicable, a confidential treatment request to request confidential treatment for this Agreement and proposed redacted version of this Agreement, and the other Party agrees to promptly (and in any event, no less than [***] Business Days after receipt of such request and, if applicable, proposed redactions) give its input in a reasonable manner in order to allow the Party seeking disclosure to file its request within the time lines prescribed by applicable SEC regulations. The Party seeking such disclosure shall exercise Commercially Reasonable Efforts to obtain confidential treatment of this Agreement from the SEC as represented by the redacted version reviewed by the other Party.

(b) Further, each Party acknowledges that the other Party may be legally required, or may be required by the listing rules of any exchange on which the other Party's or its Affiliate's securities are traded or advised by its counsel, to make public disclosures (including in filings with the SEC or other agency) of certain material developments or material information generated under this Agreement and agrees that each Party may make such disclosures as required by law, listing rules or advice; provided that the Party seeking such disclosure shall provide the other Party with a copy of the proposed text of such disclosure sufficiently in advance of the scheduled release to afford such other Party a reasonable opportunity to review and comment thereon.

(c) If either Party desires to issue a press release or make a public announcement concerning the material terms of this Agreement or the Development, Commercialization or Exploitation of the Compounds or a Licensed Product under this

Agreement, such as the achievement of Regulatory Approvals of the Licensed Product or data from a clinical trial, such Party shall provide the other Party with the proposed text of such announcement for prior review and, except to the extent such press release or public announcement is permitted by subsection (a) or (b) above, approval by such other Party.

(d) The Parties agree that after a public disclosure has been made or a press release or other public announcement has been issued in compliance with subsection (a), (b) or (c) hereof, each Party may make subsequent public disclosures or issue press releases or other public announcements disclosing the same content without having to obtain the other Party's prior consent and approval.

10.6 Reporting of Financial Information. From and after the Effective Date, to the extent required by the SEC in connection with Everest or an Affiliate of Everest registering securities in a public offering, Spero Parent shall (a) cooperate with Everest or its Affiliates and their respective accountants and auditors by providing copies of books, and records related to the Licensed Products as Everest may reasonably request in connection with the preparation by Everest or its Affiliates of historical and pro forma financial statements related to the Licensed Products as may be required to be included in any filing made by Everest or any of its Affiliates under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, and the regulations promulgated thereunder, including Regulation S-X and (b) without limiting the foregoing, shall provide Everest with such information as is required for Everest or its Affiliates to prepare audited "carve out" financial statements related to the Licensed Products, for the [***] Fiscal Years prior to the Effective Date (or such shorter period as agreed to by Everest) and information requested by Everest and reasonably necessary to prepare any applicable pro forma financial information required to be filed by Everest with the SEC. Everest may also derive such "carve out" financial statements from Spero Parent's historical financial statements and accurately present in all material respects the financial position of the Licensed Products in the Licensed Field in the Territory as of the dates thereof. Everest shall (i) submit to NPLH any proposed filing containing or incorporating by reference any financial statements provided to Everest under this Section 10.6 (Reporting of Financial Information) as far in advance as reasonably practicable (and in no event, unless inconsistent with Applicable Laws, less than [***] Business Days prior to the anticipated date of filing) so as to provide NPLH a reasonable opportunity to comment thereon and (ii) in good faith consider incorporating such comments. Everest shall reimburse NPLH for all costs and expenses incurred by or on account of NPLH in connection with its compliance with this Section 10.6 (Reporting of Financial Information). All information of NPLH obtained by or on behalf of Everest under this Section 10.6 (Reporting of Financial Information) shall be deemed Confidential Information of NPLH.

10.7 Privileged Communications. In furtherance of this Agreement, it is expected that the Parties may, from time to time, disclose to one another privileged communications with counsel, including opinions, memoranda, letters and other written, electronic and verbal communications. Such disclosures are made with the understanding that they shall remain confidential in accordance with this ARTICLE 10 (Confidentiality; Publication), that they will not be deemed to waive any applicable attorney-client or attorney work product or other privilege and that they are made in connection with the shared community of legal interests existing between NPLH and Everest, including the community of legal interests in avoiding

infringement of any valid, enforceable patents of Third Parties and maintaining the validity of the Licensed Patents, Everest Patents and Joint Patents. In the event of any litigation (or potential litigation) with a Third Party related to this Agreement or the subject matter hereof, the Parties shall, upon either Party's request, enter into a reasonable and customary joint defense or common interest agreement. In any event, each Party shall consult in a timely manner with the other Party before engaging in any conduct (e.g., producing Information or documents) in connection with litigation or other proceedings that could conceivably implicate privileges maintained by the other Party. Notwithstanding anything contained in this Section 10.7(Privileged Communications), nothing in this Agreement shall prejudice a Party's ability to take discovery of the other Party in disputes between them relating to the Agreement and no information otherwise admissible or discoverable by a Party shall become inadmissible or immune from discovery solely by this Section 10.7 (Privileged Communications).

ARTICLE 11
TERM AND TERMINATION

11.1 Term. Unless earlier terminated as permitted by this Agreement, the initial term of this Agreement (the "**Initial Term**") will commence upon the Effective Date and continue in full force and effect, on a jurisdiction-by-jurisdiction and Licensed Product-by-Licensed Product basis, for [***] years, and, unless earlier terminated as permitted by this Agreement, shall automatically renew for successive [***] year terms (each, a "**Successive Term**"), in each case unless earlier terminated as permitted by the Agreement, until expiration of the last Royalty Term for the final Licensed Product in the Territory (the Initial Term, together with all Successive Terms, being the "**Term**"). Following the expiration (but not the earlier termination) of the Royalty Term for a Licensed Product in a jurisdiction in the Territory, the grants in Section 2.1 (Licenses to Everest) shall become exclusive, fully-paid, royalty-free, and irrevocable for such Licensed Product in such jurisdiction. For clarity, (a) upon the expiration (but not the earlier termination) of the Term, the grants in Section 2.1 (Licenses to Everest) shall become exclusive, fully-paid, royalty-free, and irrevocable in their entirety solely as to the Licensed Products in the Territory at the time of such expiration and (b) upon the expiration (but not the earlier termination) of the Term, the grant in Section 2.2 (License to NPLH) shall become an exclusive, perpetual, fully-paid, royalty-free and irrevocable license to the Everest Technology to Exploit products in the Licensed Field outside the Territory, in each case with the right to grant sublicenses.

11.2 Termination.

(a) **Automatic Termination for Nonpayment of Upfront Payment**. If Everest fails to pay Spero the upfront payment set forth in Section 8.1 (Upfront Payment) within [***] Business Days after the Effective Date; then, in any such case, this Agreement will automatically and immediately terminate.

(b) **Termination by Everest for Convenience.** At any time, Everest may terminate this Agreement, at its sole discretion and for any reason or no reason, by providing written notice of termination to NPLH, which notice includes an effective date of termination at least (i) [***] days after the date of the notice if the notice is given before the Regulatory

Approval of any Licensed Product; or (ii) [***] days after the date of the notice if the notice is given after the Regulatory Approval of any Licensed Product.

(c) **Termination for Cause.** If either NPLH or Everest believes that the other Party is in material breach of its obligations hereunder, then the non-breaching Party may deliver notice of such breach to the other Party. The allegedly breaching Party shall have (i) [***] days in the case of a payment breach and or (ii) [***] in the case of a non-payment breach, to cure such breach from the receipt of the notice. If the allegedly breaching Party fails to cure that breach within the applicable period set forth above, then the Party originally delivering the notice of breach may terminate this Agreement on written notice of termination. Any right to terminate this Agreement under this Section 11.2(c) (Termination for Cause) shall be stayed and the applicable cure period tolled in the event that, during such cure period, the Party alleged to have been in material breach shall have initiated dispute resolution in accordance with Section 14.10 (Dispute Resolution) with respect to the alleged breach, which stay and tolling shall continue until such dispute has been resolved in accordance with Section 14.10 (Dispute Resolution). If a Party is determined to be in material breach of this Agreement, the other Party may terminate this Agreement if the breaching Party fails to cure the breach within [***] days after the conclusion of the dispute resolution procedure (and such termination shall then be effective upon written notification from the notifying Party to the breaching Party).

(d) **Termination for Patent Challenge.** NPLH may terminate this Agreement upon [***] days' prior written notice to Everest if Everest or its Affiliates or its or their Sublicensees, individually or in association with any other person or entity, directly or indirectly, commences or participates in a Challenge to the validity or enforceability of any Licensed Patents, unless Everest, such Affiliate or Sublicensee dismisses or withdraws such legal action within [***] days of commencing or participation in such Challenge. Everest may terminate this Agreement upon [***] days' prior written notice to NPLH if NPLH or its Affiliates or its or their Sublicensees, individually or in association with any other person or entity, directly or indirectly, commences or participates in a Challenge to the validity or enforceability of any Everest Patents, unless NPLH, such Affiliate or Sublicensee dismisses or withdraws such legal action within [***] days of commencing or participation in such Challenge.

(e) **Termination for Bankruptcy.** This Agreement may be terminated at any time during the Term by either Party upon the other Party's filing or institution of bankruptcy, reorganization, liquidation or receivership proceedings, or upon an assignment of a substantial portion of the assets for the benefit of creditors by the other Party; provided that in the case of any involuntary bankruptcy proceeding such right to terminate shall only become effective if the Party consents to the involuntary bankruptcy or such proceeding is not dismissed within [***] days after the filing thereof.

11.3 Effect of Termination. Upon termination of this Agreement automatically or by either Party, the following consequences shall apply and shall be effective as of the effective date of such termination:

(a) Everest's license under Section 2.1 (License to Everest) shall terminate;

(b) If this Agreement is terminated automatically pursuant to Section 11.2(a) (Automatic Termination for Nonpayment of Upfront Payment), or by NPLH pursuant to Section 11.2(c) (Termination for Cause), 11.2(d) (Termination for Patent Challenge), or 11.2(e) (Termination for Bankruptcy), then Everest hereby grants to NPLH, effective only upon such termination, an exclusive (even as to Everest), royalty-free, fully-paid, perpetual and irrevocable license, with the right to grant sublicenses through multiple tiers, under the Everest Technology, Everest Development Data and Everest Regulatory Documentation, to Develop, make, have made, use, import, offer for sale, sell and otherwise Commercialize or Exploit the Compound and any product containing the Compound anywhere in the world in all fields of use.

(c) If this Agreement is terminated by Everest pursuant to Section 11.2(c) (Termination for Cause), or 11.2(e) (Termination for Bankruptcy), then NPLH may request, within [***] days of such termination, that Everest enter into good faith negotiations for no more than [***] days concerning the terms of an agreement with Everest granting to NPLH an exclusive (even as to Everest) license under the Everest Technology, Everest Development Data and Everest Regulatory Documentation. If no agreement is reached, then the license to NPLH under Section 2.2 (License to NPLH) shall terminate. If such agreement is reached, then such license agreement shall include, among other things, the following provisions:

(1) NPLH, its Affiliates and/or its or their respective sublicensees, as applicable, shall pay to Everest, on a jurisdiction-by-jurisdiction and Licensed Product-by-Licensed Product basis, non-refundable, non-creditable royalties based on the aggregate Net Sales of all Licensed Products sold by NPLH, its Affiliates and/or its or their respective sublicensees in the Territory during a Calendar Year at the rates set forth in the table below; provided that (A) [***]; and (B) the obligation to pay royalties will be imposed only once with respect to the same unit of a Qualified Product:

Calendar Year Net Sales (in Dollars) for Qualified Products in the Territory	**Royalty Rates as a Percentage (%) of Net Sales**
[***]	[***]%
[***]	[***]%

(2) Provisions substantially similar to those contained in Sections 8.5 (Royalty Adjustments) through 8.10 (Audit Dispute) shall also be included in such license agreement.

(d) If this Agreement is terminated by Everest pursuant to Section 11.2(b) (Termination by Everest for Convenience), then NPLH may, within [***] days of termination, request that Everest enter into a license agreement with NPLH, in which case NPLH and Everest shall negotiate in good faith for [***] days (or such longer period as it takes to negotiate, execute and deliver a license agreement), pursuant to which Everest grants to NPLH an exclusive (even as to Everest) license under the Everest Technology, Everest Development Data and Everest

Regulatory Documentation and in which case such license agreement shall include, among other things, the following provisions:

(1) NPLH, its Affiliates and/or its or their respective sublicensees, as applicable, shall pay to Everest, on a jurisdiction-by-jurisdiction and Licensed Product-by-Licensed Product basis, non-refundable, non-creditable royalties based on the aggregate Net Sales of all Licensed Products sold by NPLH, its Affiliates and/or its or their respective sublicensees in the Territory during a Calendar Year at the rates set forth in the table below; provided that (A) [***]; and (B) the obligation to pay royalties will be imposed only once with respect to the same unit of a Qualified Product:

Calendar Year Net Sales (in Dollars) for Qualified Products in the Territory	**Royalty Rates as a Percentage (%) of Net Sales**
[***]	[***]%
[***]	[***]%

(2) Provisions substantially similar to those contained in Sections 8.5 (Royalty Adjustments) through 8.10 (Audit Dispute) shall also be included in such license agreement.

(e) NPLH shall be solely responsible for all future worldwide Development, Manufacture and Commercialization of the Compound and Licensed Products in the Licensed Field, at its sole cost and expense.

(f) Everest shall return to NPLH or destroy, at NPLH's election, all Confidential Information of NPLH, including all copies thereof and all materials, substances and compositions delivered or provided by or on behalf of NPLH to Everest.

(g) Everest shall deliver to NPLH all Regulatory Filings and Regulatory Approvals for the Compound and any Licensed Product, all Everest Development Data and all Everest Know-How, which Regulatory Filings, Regulatory Approvals, Everest Development Data or Everest Know-how shall also be subject to the license grant in the first sentence of Section 11.3(d) (Effect of Termination - subsection (d)) above.

(h) Everest shall disclose to NPLH all Everest Know-How, Everest Development Data and all Joint Inventions to the extent not already known to NPLH, which may be necessary or reasonably useful for NPLH to continue to Develop, Manufacture and Commercialize the Compound and Licensed Products in the Licensed Field. In addition, Everest shall, at NPLH's request, provide reasonable technical assistance and transfer all Everest Know-How, Everest Development Data and Joint Inventions necessary to Manufacture the Compound or Licensed Products to NPLH or its designee.

(i) All Confidential Information of Everest relating to the Compound or any Licensed Product, including without limitation all Everest Know-How and Everest Development

Data, shall become Confidential Information of NPLH, with NPLH considered the Disclosing Party and Everest considered the Receiving Party and Everest may not rely on its or any of its Affiliates' or any Sublicensee's possession or development thereof as an exception under ARTICLE 10 (Confidentiality; Publication).

(j) Everest shall, at NPLH's request and election, use Commercially Reasonable Efforts to facilitate negotiations between NPLH and Everest's Third Party providers of clinical research, manufacturing and/or distribution services and to assign any contracts with such entities to NPLH.

(k) Everest shall, and shall cause its Affiliates and its and their Sublicensees to, promptly provide a copy to NPLH of all Licensed Product Agreements, and, to the extent requested by NPLH in writing, use reasonable efforts to assign to NPLH any Licensed Product Agreement, unless, with respect to any such Licensed Product Agreement, such Licensed Product Agreement expressly prohibits such assignment, in which case Everest (or such Affiliate or Sublicensee, as applicable) shall cooperate with NPLH in all reasonable respects to secure the consent of the applicable Third Party to such assignment, at Everest's expense;

(l) Everest shall transfer to NPLH all units of the Compound and the Licensed Products in its possession, provided that NPLH shall reimburse Everest for the Cost of Goods of such units.

(m) Everest shall, and hereby does, effective on such termination, assign to NPLH all of Everest's and its Affiliates' right, title and interest in and to any and all Product Trademarks and other trademarks used by Everest and its Affiliates in the Territory in connection with its Development, Manufacture or Commercialization of Licensed Products (excluding any such trademarks that include, in whole or part, any corporate name or logo of Everest or its Affiliates), including all goodwill therein, and Everest shall promptly take such actions and execute such instruments, assignments and documents as may be necessary to effect, evidence, register and record such assignment.

11.4 Survival. Expiration or termination of this Agreement shall not relieve any Party of any obligation accruing prior to such expiration or termination, nor shall expiration or any termination of this Agreement preclude either Party from pursuing all rights and remedies it may have under this Agreement, at law or in equity, with respect to breach of this Agreement. In addition, the provisions of ARTICLE 1 (Definitions), subclauses (b) through (d) of Section 5.4 (Rights of Reference), Section 8.8 (Taxes), Section 8.9 (Financial Records and Audit), Section 8.10 (Audit Dispute), Section 9.1 (Ownership of Intellectual Property); ARTICLE 10 (Confidentiality; Publicity), Section 11.3 (Effect of Termination), this Section 11.4 (Survival), ARTICLE 13 (Indemnification; Liability), and ARTICLE 14 (General Provisions) hereof shall survive the expiration or termination of this Agreement. In addition, in the event that the this Agreement is terminated by Everest pursuant to Section 11.2(c) (Termination for Cause) and, pursuant to Section 11.3 (Effect of Termination), either NPLH does not timely request that Everest enter into good faith negotiations concerning the terms of an agreement with NPLH granting NPLH a license under the Everest Technology and Everest Development Data, or if no agreement is timely reached, then the provisions of Sections 9.2 through 9.9 of ARTICLE 9

(Intellectual Property), solely with respect to Joint Inventions, shall also survive the expiration or termination of this Agreement.

11.5 Termination Not Sole Remedy. Termination is not the sole remedy under this Agreement and, whether or not termination is effected and notwithstanding anything contained in this Agreement to the contrary, all other remedies will remain available except as agreed to otherwise herein.

ARTICLE 12
REPRESENTATIONS AND WARRANTIES

12.1 Representations and Warranties of Each Party. Each Party represents and warrants to each other Parties as of the Effective Date that:

(a) it has the full right, power and authority to enter into this Agreement, to perform its obligations hereunder;

(b) this Agreement has been duly executed by it and is legally binding upon it, enforceable in accordance with its terms, and does not conflict with any agreement, instrument or understanding, oral or written, to which it is a party or by which it may be bound, nor violate any material law or regulation of any court, governmental body or administrative or other agency having jurisdiction over it;

(c) this Agreement is a legal, valid and binding obligation of such Party enforceable against it in accordance with its terms and conditions, subject to the effects of bankruptcy, insolvency or other laws of general application affecting the enforcement of creditor rights, judicial principles affecting the availability of specific performance and general principles of equity (whether enforceability is considered a proceeding at law or equity);

(d) it is not under any obligation, contractual or otherwise, to any Person that conflicts with or is inconsistent in any material respect with the terms of this Agreement or that would impede the diligent and complete fulfillment of its obligations hereunder; and

(e) neither it nor any of its Affiliates has been debarred or is subject to debarment and neither it nor any of its Affiliates will use in any capacity, in connection with the services to be performed under this Agreement, any Person who has been debarred pursuant to Section 306 of the FFDCA or who is the subject of a conviction described in such section.

12.2 Mutual Covenants.

(a) **Employees, Consultants and Contractors**. Each Party covenants that it has obtained or will obtain written agreements from each of its employees, consultants and contractors who perform Development activities pursuant to this Agreement, which agreements will obligate such persons to obligations of confidentiality and non-use and to assign Inventions in a manner consistent with the provisions of this Agreement.

(b) **Debarment**. Each Party represents, warrants and covenants to the other Parties that it is not debarred or disqualified under the FFDCA, as may be amended, or comparable laws in any country or jurisdiction other than the U.S., and it does not, and will not during the Term, employ or use the services of any person who is debarred or disqualified, in connection with activities relating to the Compound or any Licensed Product. In the event that any Party becomes aware of the debarment or disqualification or threatened debarment or disqualification of any person providing services to such Party, including the Party itself or its Affiliates, that directly or indirectly relate to activities contemplated by this Agreement, such Party shall immediately notify the other Parties in writing and such Party shall cease employing, contracting with, or retaining any such person to perform any such services.

(c) **Compliance**. Each Party covenants as follows:

(1) In the performance of its obligations under this Agreement, such Party shall comply and shall cause its and its Affiliates' employees and contractors to comply with all Applicable Laws, including all export control, anti-corruption and anti-bribery laws and regulations, and shall not cause such other Party's Indemnitees to be in violation of any Applicable Laws or otherwise cause any reputational harm to such other Party.

(2) Such Party and its and its Affiliates' employees and contractors shall not, in connection with the performance of their respective obligations under this Agreement, directly or indirectly through Third Parties, pay, promise or offer to pay, or authorize the payment of, any money or give any promise or offer to give, or authorize the giving of anything of value to a Public Official or Entity or other person for purpose of obtaining or retaining business for or with, or directing business to, any person, including, without limitation, either Party (and each Party represents and warrants that as of the Effective Date, such Party, and to its knowledge, its and its Affiliates' employees and contractors, have not directly or indirectly promised, offered or provided any corrupt payment, gratuity, emolument, bribe, kickback, illicit gift or hospitality or other illegal or unethical benefit to a Public Official or Entity or any other person in connection with the performance of such Party's obligations under this Agreement, and each Party covenants that it and its Affiliates' employees and contractors shall not, directly or indirectly, engage in any of the foregoing).

(3) Each Party shall have the right to suspend or terminate this Agreement in its entirety where there is a credible finding, after a reasonable investigation, that the other Party, in connection with performance of such other Party's obligations under this Agreement, has violated any anti-corruption or anti-bribery laws or regulations.

(4) Each Party shall not, during the Term, assign, transfer, convey or otherwise encumber its right, title and interest in (A) Licensed Technology, in the case of NPLH, in a manner that is inconsistent with the exclusive license granted to Everest under Section 2.1 (Licenses to Everest) or (B) Everest Technology, in the case of Everest, in a manner that is inconsistent with the exclusive license granted to NPLH under Section 2.2 (License to NPLH), in each case without the prior written consent of the other Party (which consent shall not be unreasonably withheld, conditioned or delayed)

(5) Each Party shall not grant any right to any Third Party under the (A) Licensed Technology (in the case of NPLH) that would conflict with the rights granted to Everest hereunder, or (B) Everest Technology (in the case of Everest) that would conflict with the rights granted to NPLH hereunder.

12.3 Representations and Warranties by NPLH. NPLH represents and warrants to Everest as of the Effective Date that:

(a) to NPLH's knowledge, the patents and patent applications listed on Exhibit A constitute all Licensed Patents existing as of the Effective Date (the "**Existing Licensed Patents**");

(b) NPLH has sufficient legal and/or beneficiary title, ownership or license, free and clear from any mortgages, pledges, liens, security interests, conditional and installment sales agreements, encumbrances, charges or claims of any kind, of or to the Licensed Technology to grant the license to Everest as purported to be granted under this Agreement;

(c) NPLH has not previously assigned, transferred, conveyed or otherwise encumbered its right, title and interest in the Licensed Technology in a manner that is inconsistent with the exclusive license granted to Everest under Section 2.1 (Licenses to Everest), other than encumbrances constituting Permitted Liens.

(d) The Licensed Technology is complete, accurate, effective and capable of achieving the Development and Manufacturing of the Compound and the Licensed Products. The Parties hereby irrevocably agree that the Licensed Technology shall be deemed to be complete, accurate, effective and capable of achieving the Development and Manufacturing of the Compound and the Licensed Products (and the foregoing representation and warranty shall be satisfied) if the Compound or the Licensed Products (as the case may be) is/are capable of being produced in a manner that complies with the specifications contained in (i) the technical documents NPLH provided to Everest for evaluation and (ii) IND(s) submitted to the applicable Regulatory Authority(ies).

(e) NPLH has not received any notice from a Third Party that the Development of the Compound or any Licensed Product conducted by NPLH prior to the Effective Date has infringed any Patents of any Third Party or infringed or misappropriated any other intellectual property of any Third Party. Based on NPLH's understanding as of the Effective Date of the Compound and the Licensed Products and their intended use as of the Effective Date, the Development, Manufacture, use or sale of any Compound or any Licensed Product pursuant to this Agreement does not, to the knowledge of NPLH, (y) infringe any Patents of any Third Party or (z) infringe or misappropriate any other intellectual property of any Third Party. No claim or action has been brought or, to NPLH's knowledge, threatened in writing, by any Governmental Authority or Third Party (i) that any Spero Trademark violates the rights of a Third Party or (ii) currently challenging the enforceability or validity of any Spero Trademark;

(f) NPLH has not as of the Effective Date granted any right to any Third Party under the Licensed Technology that would conflict with the rights granted to Everest hereunder;

(g) NPLH has no knowledge as of the Effective Date of any Third Party that is infringing or misappropriating any of the Licensed Technology;

(h) no claim or action has been brought or, to NPLH's knowledge, threatened in writing by any Third Party alleging that the issued patents in the Licensed Patent Rights are invalid or unenforceable, and none of the Existing Patent Rights is the subject of any interference, opposition, cancellation or other protest proceeding;

(i) with respect to any Licensed Patents for which the U.S. federal government retains rights as identified in Section 2.1(b) (Licenses to Everest - subsection (b)), NPLH has complied with all its obligations pursuant to 35 U.S.C. §§ 200-212 and 37 C.F.R. § 401 et seq., and has taken all steps required pursuant to 35 U.S.C. §§ 200-212 and 37 C.F.R. § 401 et seq. to grant the rights under such Licensed Patents to Everest as provided under 2.1 (Licenses to Everest);

(j) to NPLH's knowledge, as of the Effective Date, there is no Know-How owned or controlled by NPLH that is necessary for the Development of the Compound that is not within the Licensed Know-How; and

(k) to NPLH's knowledge, (x) all clinical trials conducted by NPLH or its Affiliates prior to the Effective Date have been in compliance in all material respects with all Applicable Laws, and (y) no data or other information generated or otherwise received from such clinical trials conducted up to the Effective Date has, or is reasonably expected to have, any materially negative impact on the Exploitation of any Licensed Product in the Territory.

12.4 Representations and Warranties by Everest. Everest represents and warrants to NPLH as of the Effective Date that:

(a) Everest has not previously assigned, transferred, conveyed or otherwise encumbered its right, title and interest in Everest Technology in a manner that is inconsistent with the exclusive license granted to NPLH under Section 2.2 (License to NPLH);

(b) Everest has not as of the Effective Date, and will not during the Term, grant any right to any Third Party under the Everest Technology that would conflict with the rights granted to NPLH hereunder;

(c) Everest has no knowledge as of the Effective Date of any Third Party that is infringing or misappropriating any of the Everest Technology;

(d) no claim or action has been brought or, to Everest's knowledge, threatened in writing by any Third Party alleging that the Everest Patents are invalid or unenforceable, and no Everest Patent is the subject of any interference, opposition, cancellation or other protest proceeding;

(e) to Everest's knowledge, as of the Effective Date, there is no Know-How necessary for the Development of the Compound or the Licensed Products that is Controlled by any Third Party; and

(f) as of the Effective Date, Everest has the capability to, and reasonably believes it has or will have sufficient access to the financial resources necessary to, perform its obligations under this Agreement, including without limitation, its obligations to (i) use Commercially Reasonable Efforts to Develop, Exploit, Commercialize and obtain Regulatory Approval for the Compounds and each Licensed Product in the Licensed Field in the Territory and (ii) make the required payments to NPLH hereunder.

12.5 No Other Warranties. EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT, NO PARTY MAKES, AND EACH PARTY EXPRESSLY DISCLAIMS, ANY AND ALL WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING THE WARRANTIES OF DESIGN, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, VALIDITY OF PATENTS, NON-INFRINGEMENT OF THE INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES, OR ARISING FROM A COURSE OF DEALING, USAGE OR TRADE PRACTICES.

ARTICLE 13
INDEMNIFICATION; LIABILITY

13.1 Indemnification by NPLH. NPLH shall indemnify, defend and hold Everest, its Affiliates, and their respective officers, directors, agents and employees ("**Everest Indemnitees**") harmless from and against any Claims against them to the extent arising or resulting from:

(a) the material breach by NPLH of this Agreement (other than a breach of Section 12.3(d));

(b) the gross negligence or willful misconduct on the part of NPLH or its Affiliates or its or their respective officers, directors, agents or employees in performing its obligations under this Agreement; or

(c) the Exploitation by NPLH or any of its Affiliates or its or their sublicensees or its or their distributors or contractors of the Compound or the Licensed Products outside the Territory;

except, in each case (a), (b) and (c) above, for those Claims for which Everest has an obligation to indemnify NPLH pursuant to Section 13.2 (Indemnification by Everest) hereof or, to the extent such Claims result from the material breach by Everest of any covenant, representation, warranty or other agreement made by Everest in this Agreement or the negligence or willful misconduct of any Everest Indemnitee. Notwithstanding the above, NPLH will have no obligation to defend or indemnify Everest or its Affiliates for any claim brought by a shareholder or a class of shareholders of Everest or its Affiliates including, but not limited to, securities fraud claims, shareholder direct claims, and shareholder derivative claims, except to the extent resulting from the gross negligence or willful misconduct on the part of NPLH or any Affiliate.

13.2 Indemnification by Everest. Everest shall indemnify, defend and hold NPLH, its Affiliates, and their respective officers, directors, agents and employees ("**NPLH Indemnities**") harmless from and against any Claims arising under or related to this Agreement against them to the extent arising or resulting from:

(a) the material breach by Everest of this Agreement;

(b) the gross negligence or willful misconduct on the part of Everest or its Affiliates or its or their respective officers, directors, agents or employees in performing its obligations under this Agreement; or

(c) the Exploitation by Everest or any of its Affiliates or its or their Sublicensees or its or their distributors or contractors of the Compound or the Licensed Products in the Territory;

except, in each case (a), (b) and (c) above, those Claims for which NPLH has an obligation to indemnify Everest pursuant to Section 13.1 (Indemnification by NPLH) hereof or, to the extent such Claims result from the material breach by NPLH of any covenant, representation (other than the representation set forth in Section 12.3(d), warranty or other agreement made by NPLH in this Agreement or the negligence or willful misconduct of any NPLH Indemnitee. Notwithstanding the above, Everest will have no obligation to defend or indemnify NPLH or its Affiliates for any claim brought by a shareholder or a class of shareholders of NPLH or its Affiliates including, but not limited to, securities fraud claims, shareholder direct claims, and shareholder derivative claims, except to the extent resulting from the gross negligence or willful misconduct on the part of Everest or any Affiliate.

13.3 Indemnification Procedure

(a) **Notice of Claim**. All indemnification claims in respect of a Party, its Affiliates or their respective directors, officers, employees and agents shall be made solely by such Party to this Agreement (the "**Indemnified Party**"). The Indemnified Party shall give the other Party (the "**Indemnifying Party**") a prompt written notice (an "**Indemnification Claim Notice**") of any Claims or discovery of fact upon which such Indemnified Party intends to base a request for indemnification under this ARTICLE 13 (Indemnification; Liability), but in no event shall the Indemnifying Party be liable for any Claims to the extent that such Claims result from any delay in providing such notice. Each Indemnification Claim Notice must contain a description of the Claim and the nature and amount of such Claim (to the extent that the nature and amount of such Claim is known at such time).

(b) **Control of Defense**. The Indemnifying Party shall have the right to assume the defense of any Claim by giving written notice to the Indemnified Party within [***] days after the Indemnifying Party's receipt of an Indemnification Claim Notice. The assumption of the defense of a Claim by the Indemnifying Party shall not be construed as an acknowledgment that the Indemnifying Party is liable to indemnify the Indemnified Party in respect of the Claim, nor shall it constitute a waiver by the Indemnifying Party of any defenses it may assert against the Indemnified Party's claim for indemnification. Upon assuming the defense of a Claim, the Indemnifying Party may appoint as lead counsel in the defense of the

Claim any legal counsel selected by the Indemnifying Party; provided that it obtains the prior written consent of the Indemnified Party (which consent shall not be unreasonably withheld, conditioned or delayed). In the event the Indemnifying Party assumes the defense of a Claim, upon the Indemnifying Party's relevant notice the Indemnified Party shall immediately deliver to the Indemnifying Party all original notices and documents (including court papers) received by the Indemnified Party in connection with the Claim. Should the Indemnifying Party assume the defense of a Claim, except as provided in Section 13.3(c) (Right to Participate in Defense), the Indemnifying Party shall not be liable to the Indemnified Party for any legal expenses subsequently incurred by such Indemnified Party in connection with the analysis, defense or settlement of the Claim unless specifically requested and approved in writing by the Indemnifying Party. In the event that it is ultimately determined that the Indemnifying Party is not obligated to indemnify, defend or hold harmless the Indemnified Party from and against the Claim, the Indemnified Party shall reimburse the Indemnifying Party for any and all reasonable and verifiable out-of-pocket costs and expenses (including attorneys' fees and costs of suit) incurred by the Indemnifying Party in accordance with this ARTICLE 13 (Indemnification; Liability) in its defense of the Claim.

(c) **Right to Participate in Defense**. Any Indemnified Party shall be entitled to participate in the defense of such Claim and to employ counsel of its choice for such purpose; provided, however, that such employment shall be at the Indemnified Party's sole cost and expense unless (i) the employment thereof has been specifically authorized in writing in advance by the Indemnifying Party (in which case, the defense shall be controlled as provided in Section 13.3(b) (Control of Defense), with such provisions applying mutatis mutandis; (ii) the Indemnifying Party has failed to assume the defense and employ counsel in accordance with Section 13.3(b) (Control of Defense) (in which case the Indemnified Party shall control the defense, with the reasonable out-of-pocket expense with respect thereto borne by the Indemnifying Party); or (iii) the interests of the indemnitee and the Indemnifying Party with respect to such Claim are sufficiently adverse to prohibit the representation by the same counsel of both Parties under Applicable Laws, ethical rules or equitable principles (in which case, the Indemnified Party shall control its defense, with the reasonable out-of-pocket expense with respect thereto borne by the indemnifying Party).

(d) **Settlement**. With respect to any Claims relating solely to the payment of money damages in connection with a Claim that shall not result in the applicable indemnitee(s) becoming subject to injunctive or other relief or otherwise adversely affect the business or interests of the Indemnified Party in any manner and as to which the Indemnifying Party shall have acknowledged in writing the obligation to indemnify the applicable indemnitee hereunder, the Indemnifying Party shall have the sole right to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Claim, on such terms as the Indemnifying Party, in its sole discretion, shall deem appropriate. With respect to all other Claims in connection with Claims, where the Indemnifying Party has assumed the defense of the Claim in accordance with Section 13.3(b) (Control of Defense), the Indemnifying Party shall have authority to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Claim; provided, it obtains the prior written consent of the Indemnified Party (which consent shall not be unreasonably withheld, conditioned or delayed). If the Indemnifying Party does not assume and conduct the defense of a Claim as provided above, the Indemnified Party may defend against

such Claim; provided, that the Indemnified Party shall not settle any Claim without the prior written consent of the Indemnifying Party (which consent shall not be unreasonably withheld, conditioned or delayed).

(e) **Cooperation**. If the Indemnifying Party chooses to defend or prosecute any Claim, the Indemnified Party shall and shall cause each indemnitee to, cooperate in the defense or prosecution thereof and furnish such records, information and testimony, provide such witnesses and attend such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested by the indemnifying Party in connection therewith. Such cooperation shall include access during normal business hours afforded to the Indemnifying Party to and reasonable retention by the Indemnified Party of, records and information that are reasonably relevant to such Claim and making the Indemnified Party, the indemnitees and other employees and agents available on a mutually convenient basis to provide additional information and explanation of any material provided hereunder and the indemnifying Party shall reimburse the Indemnified Party for all of its, its Affiliates' and its and their (sub)licensees' or their respective directors', officers', employees' and agents', as applicable, reasonable and verifiable out-of-pocket expenses in connection therewith.

(f) **Expenses**. Except as provided above, the costs and expenses, including fees and disbursements of counsel, incurred by the Indemnified Party and its Affiliates and its and their sublicensees and their respective directors, officers, employees and agents, as applicable, in connection with any Claim shall be reimbursed on a Calendar Quarter basis by the Indemnifying Party, without prejudice to the Indemnifying Party's right to contest the Indemnified Party's right to indemnification and subject to refund in the event the indemnifying Party is ultimately held not to be obligated to indemnify the Indemnified Party.

13.4 Mitigation of Loss. Each Indemnified Party will take and will procure that its Affiliates take all such reasonable steps and action as are reasonably necessary or as the Indemnifying Party may reasonably require in order to mitigate any Claims (or potential losses or damages) under this ARTICLE 13 (Indemnification; Liability). Nothing in this Agreement shall or shall be deemed to relieve any Party of any common law or other duty to mitigate any losses incurred by it.

13.5 Special, Indirect and Other Losses. EXCEPT IN THE EVENT OF A BREACH OF SECTION 2.7 (NON-DIVERSION), SECTION 2.8 (NON-COMPETE) OR ARTICLE 10 (CONFIDENTIALITY; PUBLICATION), NEITHER PARTY SHALL BE ENTITLED TO RECOVER FROM THE OTHER PARTY ANY SPECIAL, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE DAMAGES IN CONNECTION WITH THIS AGREEMENT OR ANY LICENSE GRANTED HEREUNDER; provided, however, that this Section 13.5 shall not be construed to limit either Party's indemnification obligations under Section 13.1 (Indemnification by NPLH) or Section 13.2 (Indemnification by Everest), as applicable.

13.6 Insurance. Each Party, at its own expense, shall maintain product liability and other appropriate insurance (or self-insure) in an amount consistent with sound business practice and reasonable in light of its obligations under this Agreement during the Term. Each Party shall

provide a certificate of insurance (or evidence of self-insurance) evidencing such coverage to the other Party upon request.

ARTICLE 14
GENERAL PROVISIONS

14.1 Governing Law. This Agreement shall be governed by and construed in accordance with the law of [***].

14.2 Assignment.

(a) Except as expressly provided hereunder, neither this Agreement nor any rights or obligations hereunder may be assigned or otherwise transferred by either Party without the prior written consent of the other Party (which consent shall not be unreasonably withheld); provided that either Party may assign or otherwise transfer this Agreement and its rights and obligations hereunder without the other Party's consent: (a) in connection with the transfer or sale of all or substantially all of the business or assets of such Party to which this Agreement relates to a Third Party, whether by merger, consolidation, divesture, restructure, sale of stock, sale of assets or otherwise; provided that in the event of any such transaction (whether this Agreement is actually assigned or is assumed by the acquiring party by operation of law (e.g., in the context of a reverse triangular merger)), intellectual property rights of the acquiring party to such transaction (if other than one of the Parties to this Agreement) and its Affiliates existing prior to the transaction shall not be included in the technology licensed hereunder; or (b) to an Affiliate, provided that the assigning Party shall remain liable and responsible to the non-assigning Party hereto for the performance and observance of all such duties and obligations by such Affiliate; and provided, further, that in any such case the assigning Party shall provide written notice to the other Party within [***] calendar days after such assignment or transfer. The rights and obligations of the Parties under this Agreement shall be binding upon and inure to the benefit of the successors and permitted assigns of the Parties, and the name of a Party appearing herein will be deemed to include the name of such Party's successors and permitted assigns to the extent necessary to carry out the intent of this section. Any assignment not in accordance with this Section 14.2 (Assignment) shall be null and void.

(b) The rights to Information, materials and intellectual property:

(1) Controlled by a Third Party permitted assignee of a Party that immediately prior to such assignment (other than as a result of a license or other grant of rights, covenant or assignment by such Party or its Affiliates to, or for the benefit of, such Third Party); or

(2) Controlled by an Affiliate of a Party that becomes an Affiliate through any Change of Control of such Party that were Controlled by such Affiliate (and not such Party) immediately prior to such Change of Control (other than as a result of a license or other grant of rights, covenant or assignment by such Party or its other Affiliates to, or for the benefit of, such Affiliate);

shall, in each of cases (1) and (2) above, be automatically excluded from the rights licensed or granted to the other Party under this Agreement.

14.3 Entire Agreement; Modification. This Agreement is both a final expression of the Parties' agreement and a complete and exclusive statement with respect to all of its terms. This Agreement supersedes all prior and contemporaneous agreements and communications, whether oral, written or otherwise, concerning any and all matters contained herein. No amendment, modification, release or discharge shall be binding on the Parties unless in writing and duly executed by authorized representatives of each of NPLH and Everest; provided that, pursuant to the definition of "Spero Trademarks" herein, NPLH or Spero Parent may designate in a writing to Everest from time to time such other Trademarks, names and logos as NPLH or Spero Parent, as the case may be, may reasonably determine. In the event of any inconsistencies between this Agreement and any schedules or other attachments hereto, the terms of this Agreement shall control.

14.4 Relationship among the Parties. The Parties' relationship with one another, as established by this Agreement, is solely that of independent contractors. This Agreement does not create any partnership, joint venture or similar business relationship between the Parties. Neither Party is a legal representative of the other Party. Neither Party can assume or create any obligation, representation, warranty or guarantee, express or implied, on behalf of the other Party for any purpose whatsoever. All persons employed by a Party shall be employees of such Party and not of the other Party and all costs and obligations incurred by reason of any such employment shall be for the account and expense of such first Party.

14.5 Non-Waiver. The failure of a Party to insist upon strict performance of any provision of this Agreement or to exercise any right arising out of this Agreement shall neither impair that provision or right nor constitute a waiver of that provision or right, in whole or in part, in that instance or in any other instance. Any waiver by a Party of a particular provision or right shall be in writing, shall be as to a particular matter and, if applicable, for a particular period of time and shall be signed by such Party. The rights and remedies provided herein are cumulative and do not exclude any other right or remedy provided by Applicable Law or otherwise available except as expressly set forth herein.

14.6 Force Majeure. Neither Party shall be held liable or responsible to the other Party or be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement (other than an obligation to make payments) when such failure or delay is caused by or results from events beyond the reasonable control of the non-performing Party, including fires, floods, earthquakes, hurricanes, embargoes, shortages, epidemics, quarantines, war, acts of war (whether war be declared or not), terrorist acts, insurrections, riots, civil commotion, strikes, lockouts or other labor disturbances (whether involving the workforce of the non-performing Party or of any other Person), acts of God or acts, omissions or delays in acting by any governmental authority (including expropriation, seizure of works, requisition, nationalization, exercise of march-in rights or compulsory licensing, except to the extent such delay results from the breach by the non-performing Party or any of its Affiliates of any term or condition of this Agreement) and any material change in the Applicable Laws of a Regulatory Authority that results in a development, clinical or regulatory delay of [***] Business

Days of more. The non-performing Party shall notify the other Party of such force majeure within [***] Business Days after such occurrence by giving written notice to the other Party stating the nature of the event, its anticipated duration and any action being taken to avoid or minimize its effect. The suspension of performance shall be of no greater scope and no longer duration than is necessary and the non-performing Party shall use Commercially Reasonable Efforts to remedy its inability to perform.

14.7 Export Control. This Agreement is made subject to any restrictions concerning the export of products or technical information from the United States or other countries that may be imposed on the Parties from time to time. Each Party agrees that it will not export, directly or indirectly, any technical information acquired from the other Party under this Agreement or any products using such technical information to a location or in a manner that at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so from the appropriate agency or other governmental entity in accordance with Applicable Laws. NPLH hereby undertakes to use Commercially Reasonable Efforts to obtain necessary licenses (if required) for exporting the Compound, the Licensed Products and the Licensed Technology from the United States or other countries.

14.8 Severability. If any provision of this Agreement is held to be illegal, invalid or unenforceable under any present or future law and if the rights or obligations of either Party under this Agreement will not be materially and adversely affected thereby: (a) such provision shall be fully severable; (b) this Agreement shall be construed and enforced as if such illegal, invalid or unenforceable provision had never comprised a part hereof; (c) the remaining provisions of this Agreement shall remain in full force and effect and shall not be affected by the illegal, invalid or unenforceable provision or by its severance here from; and (d) in lieu of such illegal, invalid or unenforceable provision, there shall be added automatically as a part of this Agreement a legal, valid and enforceable provision as similar in terms to such illegal, invalid or unenforceable provision as may be possible and reasonably acceptable to the Parties. To the fullest extent permitted by Applicable Laws, each Party hereby waives any provision of law that would render any provision hereof illegal, invalid or unenforceable in any respect.

14.9 Notices. Any notice to be given under this Agreement must be in writing and delivered either (a) in person, (b) by air mail (postage prepaid) requiring return receipt, (c) by overnight courier, or (d) by e-mail with delivery and return receipts requested and confirmation of delivery thereafter, to the Party to be notified at its address(es) given below, or at any address such Party may designate by prior written notice to the other. Notice shall be deemed sufficiently given for all purposes upon the earliest of: (i) the date of actual receipt; (ii) if air mailed, [***] days after the date of postmark; (iii) if delivered by overnight courier, the next day the overnight courier regularly makes deliveries or (iv) if sent by e-mail, the date of confirmation of receipt.

If to NPLH, Potentiator or Spero Parent:

Spero Therapeutics, Inc.
675 Massachusetts Avenue, 14th Floor
Cambridge MA 02139

Attention: Ankit Mahadevia, President and CEO
Email: [***]

with a copy (which shall not constitute notice) to:

Mintz Levin Cohn Ferris Glovsky and Popeo, P.C.
One Financial Center, 40th Floor
Boston, MA 02111
Attention: Lewis J. Geffen
Email: [***]

If to Everest:

Suite 3307, Two Exchange Square
8 Connaught Place, Central
Hong Kong
Attention: Oak Ma
Fax: [***]

With a copy to:

Morrison & Foerster
33/F, Edinburgh Tower, The Landmark
15 Queen's Road Central
Hong Kong
Attention: Chuan Sun
Facsimile: [***]

14.10 Dispute Resolution.

(a) Except as provided in Section 3.3(a) or Excluded Claims as set forth in subsection 14.10(g) below, if a dispute arises within the JDC with respect to any decision under the jurisdiction of the JDC that remains unresolved pursuant to Section 3.3 (JDC Decision-Making) or otherwise between the Parties in connection with or relating to this Agreement or any document or instrument delivered in connection herewith (collectively, a "**Dispute**"), then either Party shall have the right to refer such Dispute to the Senior Officers for attempted resolution by good faith negotiations during a period of [***] Business Days. Any final decision mutually agreed to in writing by the Senior Officers shall be conclusive and binding on the Parties.

(b) The Senior Officers shall negotiate in good faith and use reasonable efforts to settle any Dispute arising from or related to this Agreement or the breach thereof within such [***] Business-Day period. Subject to Section 14.10(h) (Dispute Resolution - subsection (h)), in the event the Senior Officers cannot fully resolve or settle such Dispute within such period, and a Party wishes to pursue the matter further, each such Dispute that is not an Excluded Claim (defined in Section 14.10(g) (Dispute Resolution - subsection (g)) below) shall

be finally resolved by binding arbitration administered by the [***] arbitration rules then in effect.

(c) The arbitration shall be conducted by a panel of three (3) neutral arbitrators experienced in the pharmaceutical business, none of whom shall be a current or former employee or director, or a current stockholder, of either Party or any of their respective Affiliates or any Sublicensee. Within [***] days after initiation of arbitration, each Party shall select [***] person to act as arbitrator and the [***] Party-selected arbitrators shall select a [***] arbitrator within [***] days of their appointment. If the arbitrators selected by the Parties are unable or fail to agree upon the [***] arbitrator, the [***] arbitrator shall be appointed by [***] (or its successor entity) in accordance with the then-current [***] arbitration rules, except as modified in this Agreement. The place of arbitration shall be in [***], and all proceedings and communications shall be in English. The procedures for the taking of evidence shall be governed by the [***]. The decision or award rendered by the Arbitrators shall be final, binding, conclusive and non-appealable, and judgment may be entered upon it in accordance with Applicable Laws in the [***] or any other court of competent jurisdiction.

(d) Either Party may apply to the arbitrators for interim injunctive relief until the arbitration award is rendered or the controversy is otherwise resolved. The arbitrators' authority to award punitive or any other type of damages not measured by a Party's compensatory damages shall be subject to the limitation set forth in Section 13.5 (Special, Indirect and Other Losses). Each Party shall bear its own costs and expenses and attorneys' fees and an equal share of the arbitrators' fees and any administrative fees of arbitration.

(e) Except to the extent necessary to confirm or enforce an award or as may be required by law, neither Party nor an arbitrator may disclose the existence, content, or results of an arbitration without the prior written consent of the other Party. In no event shall an arbitration be initiated after the date when commencement of a legal or equitable proceeding based on the dispute, controversy or claim would be barred by the applicable [***] statute of limitations.

(f) The Parties agree that, in the event of a dispute over the nature or quality of performance under this Agreement, neither Party may terminate this Agreement until final resolution of the dispute through arbitration or other judicial determination. The Parties further agree that any payments made pursuant to this Agreement pending resolution of the dispute shall be refunded if an arbitrator or court determines that such payments are not due.

(g) As used in this Section, the term "**Excluded Claim**" means a dispute, controversy or claim that concerns the construction, scope, validity, enforceability, inventorship or infringement of a patent, patent application, trademark or copyright.

(h) Nothing contained in this Agreement shall deny either Party the right to seek injunctive or other equitable relief from a court of competent jurisdiction in the context of a *bona fide* emergency or prospective irreparable harm, and such an action may be filed and maintained notwithstanding any ongoing discussions between the Parties or any ongoing arbitration proceeding. In addition, either Party may bring an action in any court of competent

jurisdiction to resolve disputes pertaining to the construction, scope, validity, enforceability, inventorship or infringement of a patent, p atent application, trademark or copyright, and no such claim shall be subject to arbitration pursuant to subsections (b) and (c) of this Section 14.10 (Dispute Resolution). Both Parties agree to waive any requirement that the other (i) post a bond or other security as a condition for obtaining any such relief; or (ii) show irreparable harm, balancing of harms, consideration of the public interest or inadequacy of monetary damages as a remedy.

14.11 Performance by Affiliates. Each Party may discharge any obligations and exercise any rights hereunder through any of its Affiliates, including without limitation the obligations of NPLH may be fulfilled by employees of Spero Parent. Each Party hereby guarantees the performance by its Affiliates of such Party's obligations under this Agreement, and shall cause its Affiliates to comply with the provisions of this Agreement in connection with such performance. Any breach by a Party's Affiliate of any of such Party's obligations under this Agreement shall be deemed a breach by such Party, and the other Party may proceed directly against such Party without any obligation to first proceed against such Party's Affiliate.

14.12 Headings. The captions to the several Articles, Sections and subsections hereof are not a part of this Agreement, but are merely for convenience to assist in locating and reading the several Articles and Sections hereof.

14.13 Waiver of Rule of Construction. Each Party has had the opportunity to consult with counsel in connection with the review, drafting and negotiation of this Agreement. Accordingly, the rule of construction that any ambiguity in this Agreement shall be construed against the drafting Party shall not apply.

14.14 Business Day Requirements. In the event that any notice or other action or omission is required to be taken by a Party under this Agreement on a day that is not a Business Day then such notice or other action or omission shall be deemed to require to be taken on the next occurring Business Day.

14.15 English Language. This Agreement has been prepared in the English language, and the English language shall control its interpretation. In addition, all notices required or permitted to be given hereunder, and all written, electronic, oral or other communications between the Parties regarding this Agreement shall be in the English language

14.16 No Benefit to Third Parties. Except as provided in ARTICLE 13 (Indemnification; Liability), the covenants and agreements set forth in this Agreement are for the sole benefit of the Parties hereto and their successors and permitted assigns and they shall not be construed as conferring any rights on any other Persons.

14.17 Further Assurances. Each Party shall duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents and instruments, as may be necessary or as the other Party may reasonably request in connection with this Agreement or to carry out more effectively the provisions and purposes hereof or to better assure and confirm unto such other Party its rights and remedies under this Agreement.

14.18 Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument

{Remainder of page intentionally left blank}

IN WITNESS WHEREOF, the Parties intending to be bound have caused this License Agreement to be executed by their duly authorized representatives.

Everest Medicines II Limited

By: /s/ Fu Wei
Name: Fu Wei
Title: Director
Date: 1/4/2019

New Pharma License Holdings, Limited

By: /s/ Ankit Mahadevia
Name: Ankit Mahadevia
Title: Director
Date: 1/4/2019

Solely for the purpose of Sections 2.3(d) and 2.12

Spero Potentiator, Inc.

By: /s/ Ankit Mahadevia
Name: Ankit Mahadevia
Title: Chief Executive Officer
Date: 1/4/2019

LIST OF EXHIBITS

Exhibit A: Licensed Patents Existing as of the Effective Date

Reference	Territory	Application No.	Publication No.	Status	Filing Date	Assignee
[***]						
[***]	[***]	[***]	[***]	[***]	[***]	[***]
	[***]	[***]	[***]	[***]	[***]	[***]
	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]
	[***]	[***]	[***]	[***]	[***]	[***]
	[***]	[***]	[***]	[***]	[***]	[***]
[***]						
[***]	[***]	[***]	[***]	[***]	[***]	[***]

Exhibit B: Spero Trademarks

JURISDICTION	[***]
SERIAL NUMBER	[***]
MARK INFORMATION	
***MARK**	[***]
STANDARD CHARACTERS	[***]
USPTO-GENERATED IMAGE	[***]
LITERAL ELEMENT	[***]
MARK STATEMENT	[***]

JURISDICTION	[***]
SERIAL NUMBER	[***]
MARK INFORMATION	
***MARK**	[***]
SPECIAL FORM	[***]
USPTO-GENERATED IMAGE	[***]
COLOR MARK	[***]
***DESCRIPTION OF THE MARK (and Color Location, if applicable)**	[***]

Exhibit C: SPR206

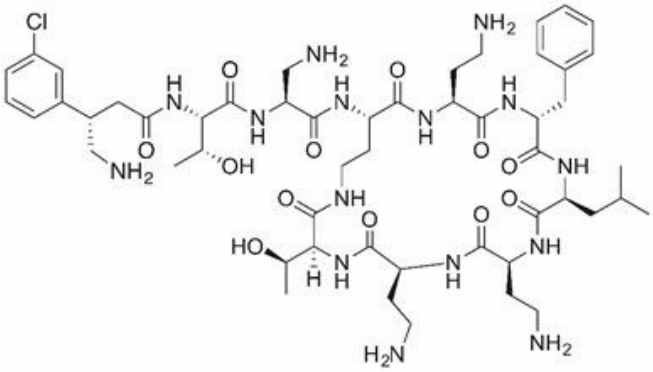


Exhibit D: SPR741

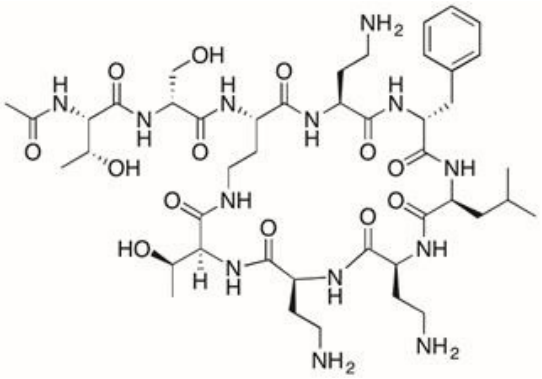


Exhibit E: Initial Development Plan

[***, 4 pages]

84849401v.1

Portions of the exhibit, indicated by the mark "[***]," were omitted and have been filed separately with the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

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 Statements on Form S-3 (No. 333-228661) and Form S-8 (No. 333-222060) of Spero Therapeutics, Inc. of our report dated March 14, 2019 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 14, 2019

Exhibit 31.1

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

I, Ankit Mahadevia, M.D., certify that:

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

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

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

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

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

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the 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: March 14, 2019

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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

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

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

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

Date: March 14, 2019

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, 2018, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

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

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

Date: March 14, 2019

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, 2018, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

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

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

Date: March 14, 2019

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