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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2020

or

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

Commission file number 001-38266

SPERO THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

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

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

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

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

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

None

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

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

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

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

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

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

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

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the 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 30, 2020, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $256.2 million (based on the last reported sale price on the Nasdaq Global Market as of such date). As of March 8, 2021, there were 29,504,257 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 2021 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2020. 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;
- the timing and outcome of the New Drug Application approval process for tebipenem HBr;
- 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 direct and indirect impact of the pandemic caused by an outbreak of a new strain of coronavirus, or COVID-19, on our business and operations, including manufacturing, research and development costs, clinical trials, regulatory processes and employee expenses;
- 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;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates;
- our ability to enter into strategic arrangements and/or collaborations and the potential benefits of such arrangements;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- our ability to continue as a going concern;
- our financial performance;
- developments relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under Part I, Item 1A. “Risk Factors”.

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

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

Risk Factor Summary

We are providing the following summary of the risk factors contained in this Annual Report on Form 10-K to enhance the readability and accessibility of our risk factor disclosures. We encourage you to carefully review the full risk factors contained in this Annual Report on Form 10-K in their entirety for additional information regarding the material factors that make an investment in our securities speculative or risky. These risks and uncertainties include, but are not limited to, the following:

- The outbreak of the novel strain of coronavirus, SARS-CoV-2, which causes COVID-19, could adversely impact our business, including our preclinical studies and clinical trials.
- We have not generated any revenue from the sale of our products, have a history of losses and expect to incur substantial future losses. The report of our auditor on our consolidated financial statements expresses substantial doubt about our ability to continue as a going concern; if we are unable to obtain additional capital, we may not be able to continue our operations on the scope or scale as currently conducted, and that could have a material adverse effect on our business, results of operations and financial condition.
- We 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.
- We are heavily dependent on the success of tebipenem HBr, which is still under development, and our ability to develop, obtain marketing approval for and successfully commercialize tebipenem HBr. If we are unable to develop, obtain marketing approval for and successfully commercialize tebipenem HBr, or if we experience significant delays in doing so, our business could be materially harmed.
- If clinical trials of our product candidates 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 such product candidates.
- To support our accelerated clinical development strategy for tebipenem HBr, we are relying, in part, on clinical data from two exploratory Phase 2 clinical trials conducted by Meiji (ME1211) and Global Pharma (L-084 04) in Japan, which were not conducted in accordance with FDA guidance for clinical trials in patients with cUTI. To the extent that these clinical trial design differences limit our use of the clinical data, our proposed clinical trial plan for tebipenem HBr with the FDA could be materially delayed and we may incur material additional costs.
- Preliminary or interim data from our clinical studies that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- Serious adverse events or undesirable side effects or other unexpected properties of tebipenem HBr or any other product candidate may be identified during development or after approval that could delay, prevent or cause the withdrawal of regulatory approval, limit the commercial potential, or result in significant negative consequences following marketing approval.
- 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.
- If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing tebipenem HBr or any other product candidate if such product candidate is approved.
- We face substantial competition from other pharmaceutical and biotechnology companies and our operating results may suffer if we fail to compete effectively.
- 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.
- 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.

- 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.
- 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.
- We have registered trademarks and pending trademark applications. Failure to enforce our registered marks or secure registration of our pending trademark applications could adversely affect our business.
- If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize tebipenem HBr or our other product candidates, and our ability to generate revenue will be materially impaired.

Item 1. Business.

Overview

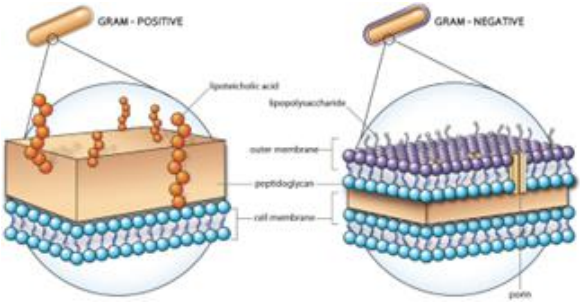
We are a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing and commercializing treatments in high unmet need areas involving multi-drug resistant, or MDR, bacterial infections and rare diseases. Our most advanced product candidate, Tebipenem Pivoxil Hydrobromide,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

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

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 U.S. Centers for Disease Control's Antibiotic Resistance Threats in the United States, 2019 report, more than 2.8 million antibiotic-resistant infections occur in the United States each year, and more than 35,000 people die as a result. Approximately 70% of the pathogens that cause these infections are resistant to at least one antibiotic used to treat them. Resistance rates are climbing in both hospital-acquired and community-acquired infections. According to UNC Infectious Diseases investigator David van Duin, MD, PhD 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 Centers for Disease Control and Prevention, or CDC, estimates that the annual impact of antibiotic-resistant infections on the United States economy is $20-35 billion in excess direct health care costs.

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 World Health Organization, or WHO, published a list of Gram- negative bacteria based on the urgency of need for new antibiotics and highlighted a critical group of MDR Gram-negative bacteria that pose a particular threat to human health, including *Acinetobacter*, *Pseudomonas* and multiple Enterobacteriaceae (including *Klebsiella sp.*, *E. coli*, *Serratia* and *Proteus*). These pathogens are associated with significant mortality because the increased incidence of antibiotic resistance has limited the number of effective treatment options.

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

Chronic Bacterial Infection without a Viable Cure

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

Although rare, the incidence of pulmonary NTM disease is increasing worldwide. It is estimated that approximately 130,000 patients suffer from NTM disease in the United States and Europe, a figure that is growing at a rate of 8% annually. In addition, many patients go undiagnosed and could benefit from treatment with additional testing. The elderly and people with compromised immune or lung function are at greatest risk, as are patients with bronchiectasis for whom it is estimated that up to 50% may also have active lung infection caused by NTM. Treatment of pulmonary NTM disease requires prolonged therapy (continuing for approximately 12 to 24 months) with a combination regimen and is frequently complicated by tolerability and/or toxicity issues. Additionally, there are currently no oral antibiotics specifically approved for use to treat pulmonary NTM disease. *M. avium* complex is the most common NTM to cause human infection in the United States, and it makes up around 80% of the infections.

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

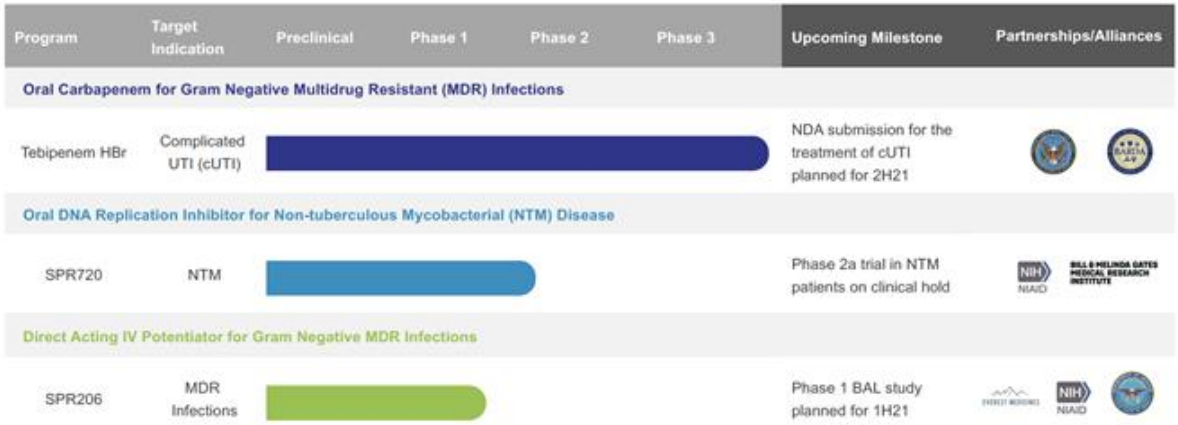
Our Solution

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

- ***Tebipenem HBr is designed to address the lack of orally administrable antibiotics to prevent hospitalization and permit IV-to-oral switch therapy in resistant Gram-negative infections***. Resistance to most commonly used classes of oral antibiotics, such as cephalosporins and fluoroquinolones, has increased significantly. Many of the most commonly used antibiotics for MDR Gram-negative infections are only available in an IV-administered formulation. Treatment with effective orally administrable antibiotics may prevent hospitalizations for serious infections and enable earlier, more convenient and cost-effective treatment of patients following hospitalization. Tebipenem HBr is an orally administrable tablet that we believe has the potential, if approved, to treat such infections in both the community and hospital settings, thereby preventing certain hospitalizations and enabling patients to transition to oral treatment. In the community setting, tebipenem HBr, if successfully developed and approved, may allow patients who develop an infection with a resistant pathogen, but are stable enough to be treated in the community, to avoid the need for an IV catheter and even hospitalization. Hospitalization is a key cost driver for hospital systems and payers, with increasing emphasis being placed on hospital avoidance. In the hospital setting, the lack of effective oral stepdown options results in the potential for lengthy hospital stays or the insertion of a peripherally inserted central catheter, or PICC, to facilitate outpatient administration of IV antibiotics. Tebipenem HBr may enable faster discharges, providing cost-saving advantages for the hospital and mitigating the risk of catheter-related and other hospital-acquired infections for patients.
- ***SPR720 is designed to be the first oral treatment for NTM infection where treatment failure is common and no approved therapies exist***. The current treatment for NTM infection is lengthy and involves combination therapy, often including three or more antibiotics, including injectables. None of these combination treatments are currently approved for use in NTM infection. Treatment failure is common and is often due to poor compliance or patients' inability to tolerate the regimen. Many patients experience progressive lung disease as a result of NTM infection, and mortality rates are high, ranging from 29% to 69% within five years of diagnosis. We believe SPR720, if successfully developed, has the potential to be the first approved oral agent for NTM pulmonary infection. We initiated a Phase 2a clinical trial in patients with NTM pulmonary disease in December 2020 based on data from the Phase 1 clinical trial, pharmacokinetic analyses and preclinical studies supporting its advancement. On February 5, 2021, we announced that the FDA informed us that a clinical hold had been placed on our Phase 2a clinical trial of SPR720, which is further described elsewhere in this "Business" section of our Annual Report on Form 10-K under the heading "Update on Phase 2a Clinical Trial."
- ***SPR206 is designed to address the decline in the ability 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 be developed as a single drug.

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

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



Our Product Candidates

Tebipenem HBr (tebipenem pivoxil hydrobromide): Novel Antibiotic with Potential to be the First Oral Carbapenem for Use in Adults

Our lead product candidate, tebipenem HBr, is an oral carbapenem intended for use in adults to treat MDR Gram-negative infections. In September 2020, we announced positive top-line data from the single pivotal Phase 3 clinical trial, which is entitled ADAPT-PO, that is required for approval of tebipenem HBr to treat complicated urinary tract infection, or cUTI, and acute pyelonephritis, or AP. The ADAPT-PO trial achieved its primary objective, demonstrating that oral tebipenem HBr was statistically non-inferior to intravenous ertapenem in the treatment of patients with cUTI and patients with AP with respect to the primary endpoint of overall response at the test-of-cure, or TOC, visit in the microbiological-intent-to-treat, or micro-ITT, population. Comparative safety and tolerability data from 1,372 hospitalized adult patients enrolled in the study were similar between the tebipenem HBr and ertapenem treatment groups. The ADAPT-PO trial was designed as a double-blind, double-dummy trial to compare oral tebipenem HBr with an existing standard of care intravenous, or IV, antibiotic, ertapenem, in 1,372 hospitalized adult patients with cUTI or AP, randomized 1:1 in each arm. We intend to make a New Drug Application, or NDA, submission to the United States Food and Drug Administration, or FDA, for tebipenem HBr for the treatment of cUTI and AP in the second half of 2021.

Carbapenems have been utilized for over 30 years and are considered the standard of care for many serious MDR Gram-negative bacterial infections, but to date they have only been available as IV-administered formulations. Currently, there are no commercially available oral carbapenems for use in adults, and we believe tebipenem HBr has the potential to address this unmet need. Tebipenem HBr is an oral tablet formulation of tebipenem, a carbapenem-class antibiotic marketed by Meiji Seika Pharma Co. Ltd., or Meiji, in Japan as Orapenem® since 2009 for common pediatric infections. To accelerate our clinical development of tebipenem HBr, in June 2017 we signed an exclusive license to certain data and know-how from Meiji and a global pharmaceutical company, to which we refer as Global Pharma, which we intend to use to support our clinical development of tebipenem HBr. We have global commercialization rights to tebipenem HBr, except in certain contractually specified Asian countries.

The FDA has designated tebipenem HBr as a Qualified Infectious Disease Product, or QIDP, for the treatment of cUTI, community acquired bacterial pneumonia, or CABP, and moderate to severe diabetic foot infections, or DFI, under the Generating Antibiotics Incentives Now Act, or the GAIN Act. Among other benefits of a QIDP designation, the first marketing application for the QIDP-designated drug qualifies for priority review by the FDA. If tebipenem HBr is approved for treatment of cUTI, CABP or DFI, the QIDP designation previously granted to tebipenem HBr for those indications will entitle the drug product to receive a one-time five-year extension to any non-patent exclusivity period awarded for tebipenem HBr in the United States (the so-called GAIN exclusivity extension), 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, among other possible qualifying periods of regulatory exclusivity. 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. The QIDP designation for tebipenem HBr, however, does not guarantee a faster development process or ensure FDA approval. Tebipenem HBr has been granted Fast Track Designation by the FDA for the treatment of cUTI and AP.

In January 2021, tebipenem HBr was granted a patent covering a crystalline form and pharmaceutical compositions of tebipenem HBr, with an expiration of February 2038. We believe that our intellectual property portfolio for tebipenem HBr, which includes multiple patent applications pending, will provide tebipenem HBr protection globally, including in the United States and Europe, through 2038.

Advantages of tebipenem HBr

Key attributes of tebipenem HBr support our confidence in tebipenem HBr's commercial potential, if tebipenem HBr receives regulatory approval. We believe tebipenem HBr has the potential to be a safe and effective treatment for cUTI and other serious and life-threatening infections for which we may develop tebipenem HBr.

- ***Potential to be the first oral carbapenem in adults, if approved***. Tebipenem HBr is designed to be the first broad-spectrum oral carbapenem-class antibiotic for use in adults to treat MDR Gram-negative infections. Unlike other carbapenems, which are only available as IV-administered infusions, tebipenem HBr is an orally administered tablet. Oral administration may potentially allow physicians to avoid IV-administered antibiotics for otherwise healthy or stable patients and/or allow for a reduction in costs associated with avoiding or shortening hospitalization.
- ***Potential for differentiated launch characteristics.*** There are limited branded or generic oral options currently approved or available to treat fluoroquinolone- and cephalosporin-resistant pathogens to assist with transitioning patients from the hospital to the community setting, or to prevent unnecessary hospitalization for cUTI. We believe tebipenem HBr, if approved, would be primarily reimbursable outside the hospital diagnosis-related group, or DRG, system, because of the desire from patients, physicians and payors alike to discharge patients from the hospital. Together, we believe these factors could differentiate tebipenem HBr from other recently launched antibiotic drugs, many of which are injectable, reimbursed within the hospital DRG system, and/or substitutable with equally effective generic alternatives.
- ***Potential uses for treatment.*** As a result of extensive existing data, we believe that tebipenem HBr has the potential to be used for the treatment of cUTI and other serious and life-threatening infections caused by resistant Gram-negative pathogens.
- ***Clinical profile observed in the ADAPT-PO clinical trial suggests there are no tradeoffs in treating with oral tebipenem HBr versus IV ertapenem; safety and tolerability data supported by the Japanese experience.*** The ADAPT-PO trial achieved its primary objective, demonstrating that oral tebipenem HBr was statistically non-inferior to intravenous ertapenem in the treatment of patients with cUTI and patients with AP with respect to the primary endpoint of overall response at the TOC visit in the micro-ITT population. In the ADAPT-PO trial, the safety and tolerability profile for oral tebipenem HBr was similar to IV ertapenem. Both the type and frequency of adverse events were well balanced across treatment groups, with treatment-emergent adverse events reported in 26% of treated patients in both arms. The most commonly observed TEAEs were diarrhea and headaches. Serious adverse events occurred in 1.3% of tebipenem HBr-treated patients, none of which were considered to be drug-related, and there were no deaths reported in the study.

  A granule formulation of tebipenem has been approved for use in Japan in pediatric patients since 2009, where it has demonstrated a favorable safety and efficacy profile. Approximately 1,200 subjects were dosed with the active pharmaceutical ingredient of tebipenem HBr, tebipenem, in clinical and pharmacologic studies during development of this drug by Meiji and its partner in Japan. This data set includes 741 adults, including 88 patients with cUTIs, the initial indication for which we are developing tebipenem HBr. In each case tebipenem has demonstrated a favorable safety, pharmacokinetic and tolerability profile. In addition, Meiji has conducted a 3,540 patient post-marketing study supporting the safety and tolerability profile of tebipenem, specifically demonstrating a safety profile that aligns well with that observed across the clinical trial program and tolerability in line with other broad spectrum oral antibiotics.
- ***Potential to enable IV-to-oral transition of antibiotic treatment to assist with reduction in hospital stays and/or eliminate the need for hospitalization.*** We believe the unique oral formulation of tebipenem HBr may enable patients who begin IV-administered treatment for extended spectrum beta-lactamases in the hospital setting to transition to oral dosing of tebipenem HBr either in the hospital or upon discharge for convenient home-based care. We believe that the availability and use of an oral carbapenem as a transition therapy may eliminate hospitalization or reduce the length of a patient's hospital stay and the overall cost of care.

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

cUTIs in the United States	2019 *E. coli* Resistance Rates to Fluoroquinolones	2013-2014 *E. coli* Resistance Rates to Fluoroquinolones	2000-2004 *E. coli* Resistance Rates to Fluoroquinolones
Community Setting	21.2%	11.7%	0%
Hospital Setting	30.8%	34.5%	3.5%

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

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

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

In addition, the FDA has issued several warnings against the use of fluoroquinolones in certain patients. In particular, an FDA Advisory Committee stated in November 2015 that the risk of serious side effects caused by fluoroquinolones generally outweighs the benefits for patients with acute bacterial sinusitis, acute exacerbation of chronic bronchitis and uncomplicated UTIs, and the agency subsequently issued a drug safety communication to the public and required safety labeling revisions be made to all products within this drug class. The FDA has determined that fluoroquinolones should be reserved for use in patients with these conditions who have no alternative treatment options and safety warnings in the labeling of fluoroquinolone class products have been further strengthened over the past several years. We believe tebipenem HBr could become a potential alternative to oral fluoroquinolones based on its safety and efficacy profile.

Significant Market Opportunity for Tebipenem HBr

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

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

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

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

MDR UTIs while avoiding patient hospitalization. In addition, we believe tebipenem HBr has the potential to accelerate hospital discharge and obviate the need for continued IV-administered therapy at home by transitioning discharged patients to an at-home oral therapy. Our pivotal Phase 3 clinical trial for tebipenem HBr, ADAPT-PO, was conducted in a subset of UTIs called cUTIs, and our target focus within this group is the 2.7 million patients receiving second line or IV treatment in the United States annually. A significant majority of UTIs, including these cUTIs, are caused by a group of MDR Gram-negative bacteria called Enterobacteriaceae, which tebipenem HBr is effective against.

Tebipenem HBr Clinical Development Program

Single Pivotal Phase 3 Clinical Trial (ADAPT-PO)

In September 2020, we announced positive data from the ADAPT-PO Phase 3 trial evaluating an all oral regimen of tebipenem HBr head-to-head versus an all IV regimen of ertapenem for the treatment of adults with cUTI, including AP. The global, randomized, placebo-controlled ADAPT-PO Phase 3 clinical trial evaluated the safety and efficacy of tebipenem HBr in hospitalized adult patients with cUTI or AP. Patients were randomized (1:1) to receive tebipenem HBr (600 mg) orally every 8 hours, or ertapenem (1 g) IV every 24 hours, for a total of 7 to 10 days.

The ADAPT-PO trial achieved its primary objective, demonstrating that oral tebipenem HBr was statistically non-inferior to intravenous ertapenem in the treatment of patients with cUTI and patients with AP with respect to the primary endpoint of overall response at the TOC visit in the micro-ITT population. Overall response (combined clinical cure plus microbiological eradication) rates at TOC were 58.8% for oral tebipenem versus 61.6% for IV ertapenem (treatment difference, -3.3%; 95% confidence interval [CI]: -9.7, 3.2; -12.5% NI margin).

Data presented at IDWeek 2020 expanded on the topline data, and demonstrated that both the clinical cure and microbiological eradication rates were comparable between treatment groups at the end of treatment, or EOT, TOC and at the late follow-up, or LFU, visits. Specifically, clinical cure rates, which are the key determinant in routine clinical management of cUTI/AP patients, were >93% in both treatment groups at TOC. The high clinical cure rates at TOC were sustained through LFU (88.6% and 90% for tebipenem HBr and ertapenem, respectively), demonstrating a durable clinical response in patients with cUTI and AP. Favorable microbiological response rates at TOC were likewise comparable between treatment groups and were similarly sustained up to LFU in both treatment groups (57.2% and 58.2% for tebipenem HBr and ertapenem, respectively). There were no statistically significant differences between treatment groups in overall response rates across key subgroups of interest, including those determined by age, baseline diagnosis, and presence of bacteremia at baseline. Per pathogen microbiological response rates were generally balanced across treatment groups for the predominant uropathogens.

Comparative safety and tolerability data from 1,372 hospitalized adult patients enrolled in the study were similar between the tebipenem HBr and ertapenem treatment groups. Treatment emergent adverse events, or TEAEs, were reported in approximately 26% of patients in both treatment groups and the most commonly reported TEAEs in both treatment groups were diarrhea (5.0%) and headache (3.8%). Serious TEAEs were infrequent (1.3% for tebipenem HBr vs. 1.7% for ertapenem) and no deaths were reported in the trial. Three *Clostridioides difficile* associated TEAEs were observed in the ertapenem group, while none were observed in the tebipenem HBr group.

Based on our pre-IND, pre-Phase 3 meeting with the FDA, we believe that positive results from a single pivotal Phase 3 clinical trial of tebipenem HBr in cUTI would support the approval of tebipenem HBr for the treatment of cUTI. The primary analysis and assessment of non-inferiority was evaluated using a pre-specified -12.5% non-inferiority (NI) margin. This NI margin was a modification of the original NI margin of -10% that was discussed with the FDA because of concern that the COVID-19 pandemic could have an adverse effect on the trial. As a result, the NI margin was modified prior to database lock from the original NI margin. Data from the ADAPT-PO Phase 3 clinical trial of tebipenem HBr, together with requisite safety data, drug-drug interaction studies and other studies, will form the basis for the NDA for tebipenem HBr to treat cUTI, including acute pyelonephritis, which we plan to submit to the FDA in the second half of 2021. The ADAPT-PO clinical trial may also support marketing applications in other global regions.

QIDP Designation

The FDA has designated tebipenem HBr as a QIDP for the treatment of cUTI, CABP and DFI under the GAIN Act. Among other benefits of a QIDP designation, the first marketing application for the QIDP-designated drug qualifies for priority review by the FDA. The QIDP designation for tebipenem HBr, however, does not guarantee a faster development process or ensure FDA approval. Further, if tebipenem HBr is approved for the treatment of cUTI, CABP or DFI, the FDA's QIDP designation previously granted to tebipenem HBr for those indications will entitle the drug product to receive a one-time five-year extension to any non-patent exclusivity period awarded to tebipenem HBr in the United States, such as a five-year New Chemical Entity exclusivity granted under the Hatch-Waxman Act, among other possible periods of regulatory exclusivity that would qualify for a GAIN exclusivity extension.

Japanese Data Supporting Safety of Tebipenem

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

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

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

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

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

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

Funded Label Expansion Opportunity

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

SPR720: Novel Oral Antibiotic Designed for Treatment of Non-tuberculous Mycobacterial Pulmonary (NTM-PD) Disease

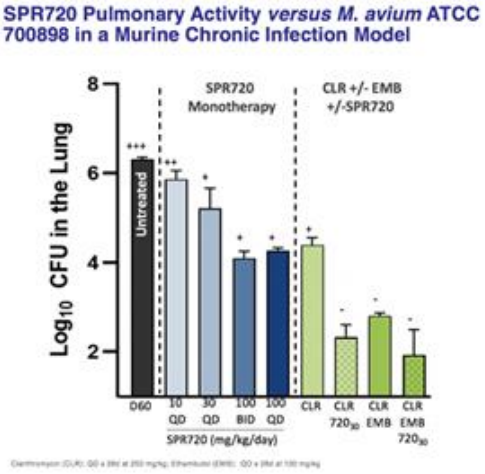
A second area of our focus is rare infectious diseases, specifically non-tuberculous mycobacterial pulmonary disease, a rare orphan disease. We are developing SPR720, which represents a novel class of antibacterial agents that target enzymes essential for bacterial DNA replication, for the treatment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

SPR720 has several key attributes including:

- ***Acceptable safety and tolerability within therapeutic dose range.*** Both the SPR720 Phase 1 trial and pharmacokinetic/pharmacodynamic (PK/PD) data for indicated that predicted therapeutic exposures could be attained with a 500 – 1,000 mg once daily oral dose. These doses in the Phase 1 trial were associated with a low incidence of adverse events with no serious adverse events reported. The most common adverse event among all cohorts was mild diarrhea not requiring discontinuation of therapy.
- ***Broad spectrum of activity.*** SPR720 has demonstrated a broad spectrum of activity in preclinical studies against the most common organisms causing NTM infections, including *Mycobacterium avium* complex, or MAC, *Mycobacterium kansasii* and *Mycobacterium abscessus*. SPR720 is applicable to both non-refractory and refractory patients.

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

SPR720 has shown potent activity against most common NTM infection species, such as *M. avium*, *M. abscessus* and *M. kansasii*. As shown in the exhibit below, SPR720 showed Pulmonary Activity versus M. avium ATCC 700898 in a Murine Chronic Infection Model. In this model SPR720 was effective as a monotherapy and in combination with SOC agents.



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 Mycobacterium avium complex, or MAC, the most common cause of NTM infections, comprising approximately 80% of all NTM infections.

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

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

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

Our SPR720 Development Plan

Our strategy is to develop SPR720 to become the first oral treatment FDA-indicated for NTM disease, and ultimately provide a treatment option to NTM patients to reduce their disease burden and improve their quality of life.

In March 2020, the FDA granted orphan drug designation for SPR720, a designation that is given to drugs intended to treat a rare disease or condition that affects fewer than 200,000 persons in the United States. An orphan drug designation can provide specific benefits including up to seven years of market exclusivity in the United States upon regulatory approval. In February 2019, we received QIDP designation for SPR720 for the treatment of lung infections caused by nontuberculous mycobacteria and for the treatment of lung infections caused by Mycobacterium tuberculosis. QIDP designation entitles a future marketing application for SPR720 for this indication to priority review by the FDA. Neither the QIDP nor orphan drug designation, however, guarantee a faster development process or ensure FDA approval. In September 2020, SPR720 was awarded Fast Track Designation by the FDA for treatment of adult patients with NTM pulmonary disease.

In December 2020, we initiated a Phase 2a dose-ranging clinical trial of SPR720 in patients with nontuberculous mycobacterial pulmonary disease following the acceptance of our investigational new drug, or IND, application for SPR720 in August 2020. The Phase 2a clinical trial is designed as a multi-center, partially blinded, placebo-controlled proof-of-concept clinical trial of SPR720 that is expected to enroll approximately 90 treatment-inexperienced patients with NTM-PD due to MAC. Patients are randomized to receive either 500 mg or 1,000 mg of oral SPR720 once daily, placebo, or standard- of-care, or SOC, consisting of a macrolide and ethambutol, plus the option of adding a rifamycin. The objectives of the trial are to evaluate the plasma pharmacokinetics, safety, tolerability, and microbiological response of SPR720 compared with placebo and SOC over 28 days of treatment, with the inclusion of the SOC arm to assess and ensure assay sensitivity for the trial design.

The doses selected for the Phase 2a trial of SPR720 are supported by pharmacokinetic analyses as well as data from the Phase 1 clinical trial of SPR720. The Phase 1 trial reported in December 2019 was designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects. Data from this Phase 1 trial was presented at ID Week 2020 and indicated that SPR720 is generally well-tolerated, and predicted therapeutic exposures could be attained with a 500 – 1,000 mg once daily oral dose.

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

Update on Phase 2a Clinical Trial

On February 5, 2021, we announced that the FDA informed us that a clinical hold had been placed on our Phase 2a clinical trial of SPR720, following our notification to the FDA of our decision to pause dosing in our ongoing Phase 2a clinical trial of SPR720 as a precautionary measure related to events in our ongoing animal toxicology study of SPR720. The decision to implement the pause was made based on a recommendation from the Company's Safety Review Board, or SRB, following review of data from an ongoing toxicology study of SPR720 in adult non-human primates in which mortalities with inconclusive causality to treatment were observed.

The animal study is being conducted to assess the potential toxicity of SPR720. A concurrent study of SPR720 in rats is proceeding uneventfully. These studies are meant to support longer-term treatment with SPR720 beyond the 28 days currently supported by IND-enabling toxicology studies. No serious adverse events have been observed in any human study participants.

Subsequent to receiving verbal notification from the FDA of the clinical hold, we received a formal clinical hold letter in which the FDA has requested additional information from the non-human primate trial, including a study report. We have decided to discontinue the Phase 2a clinical trial at this time to best facilitate future potential adjustments to the protocol based on FDA feedback and to avoid incurring costs associated with the trial while on clinical hold. We are continuing to work with the FDA to evaluate the findings and determine the further development pathway for the SPR720 clinical program.

IV Potentiator Product Candidate SPR206: Our IV-administered product candidate being developed as an innovative option to treat multi-drug resistant (MDR) Gram-negative bacterial infections in the Hospital Setting.

SPR206 is an IV-administered product candidate being developed as an innovative option to treat MDR Gram-negative bacterial infections in the Hospital Setting. Gram-negative bacteria represent a subset of bacterial organisms distinguished by the presence of an outer cell membrane. SPR206 is designed to treat MDR Gram-negative bacterial infections through interactions with the bacteria's outer cell membrane as a monotherapy.

SPR206 is a direct acting IV-administered agent that has demonstrated single-agent antibacterial activity in preclinical studies against Gram-negative bacteria, including organisms identified by the CDC and the WHO as urgent and serious threats to human health, including *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.

In January 2020 we reported results from a Phase 1 clinical trial designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects. In the Phase 1 clinical trial SPR206 was well-tolerated at doses that are likely to be within a therapeutic range for target MDR Gram-negative bacterial infections and has a safety profile that we believe supports the further development of SPR206. The Phase 1 clinical trial of SPR206 was designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects. In this SAD and MAD Phase 1 clinical trial, a total of 96 healthy volunteers were randomized to receive SPR206 or placebo. All reported adverse events were mild to moderate and there were no reported severe or serious adverse events. No evidence of nephrotoxicity was observed and there were no subjects with clinically significant changes in laboratory tests during the study. SPR206 was well-tolerated at doses up to 100 mg administered three-times a day, a total of 300 mg daily, for 14 consecutive days. Pharmacokinetic data across the cohorts indicate dose linearity and dose proportionality as well as mean plasma drug exposures of SPR206 that are concordant with preclinical models predictive for clinical efficacy against target Gram-negative pathogens.

We have conducted a preclinical toxicology study of SPR206 in accordance with good laboratory practice, or GLP, requirements as well as conducted nonclinical studies in which SPR206 demonstrated activity as a single agent against MDR and extensively drug resistant, or XDR, bacterial strains, including isolates of *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and carbapenem-resistant *Enterobacteriaceae*, in both *in vitro* and *in vivo* models of infection. We expect to initiate a Phase 1 bronchoalveolar lavage, or BAL, clinical trial to assess the penetration of SPR206 into the pulmonary compartment in the first half of 2021 and to initiate a renal impairment study of SPR206 in 2021.

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

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

SPR206 Advantages

We believe that with the following key attributes, SPR206, an IV Potentiator, has the potential to become a safe and effective treatment for serious Gram-negative infections:

- ***Potential to Expand the Potency of Standard-of-Care Antibiotics***. SPR206 is designed to expand the potency of SOC antibiotics by restoring and expanding their Gram-negative activity. We believe that this novel mechanism could provide a new option for patients with resistant Gram-negative infections, thereby improving therapeutic outcomes, decreasing physicians' reliance on older poorly tolerated and ineffective drugs.

- ***SPR206 appears to be a safe and potent IV-administered direct-acting agent***. SPR206 is designed to interact with LPS to disrupt the outer membrane. SPR206 is also designed to have direct antibiotic activity, while retaining Potentiator activity, including activity against *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Data from SPR206 *in vitro* and *in vivo* GLP safety pharmacology and absorption, distribution, metabolism, and excretion, or ADME, studies and 14-day, two-species GLP toxicology studies provide support for an acceptable safety profile, which led to SPR206's designation as a clinical candidate and the initiation of a Phase 1 clinical trial in December 2018. Phase 1 data demonstrates that SPR206 is well-tolerated at doses that are likely to be within a therapeutic range for target MDR Gram-negative bacterial infections and has a safety profile that we believe supports the further development of SPR206. We are developing SPR206 as a treatment for high-risk patients with suspected or known Gram-negative infections such as carbapenem-resistant *Enterobacteriaceae*, or CRE, carbapenem resistant *Acinetobacter baumannii*, or CRAB, and MDR *Pseudomonas aeruginosa*, or MDR PA, to prevent mortality and reduce the length of stay in the hospital setting.

SPR206—Development Plan

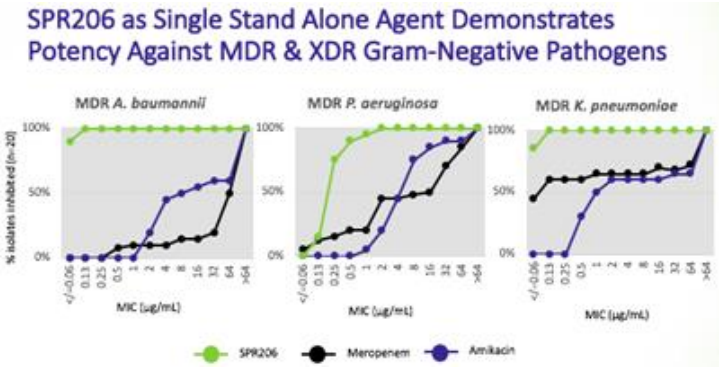
Advancing SPR206 into Two Phase 1 Clinical Trials in 2021

We plan to advance SPR206 into a Phase 1 BAL clinical trial to assess the penetration of SPR206 into the pulmonary compartment in the first half of 2021 and to initiate a renal impairment study of SPR206 in 2021.

Its advancement is supported by the Phase 1 SAD and MAD that we reported data for in January 2020. The Phase 1 trial was designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects. In the Phase 1 clinical trial, SPR206 was well-tolerated at doses that are likely to be within a therapeutic range for target MDR Gram-negative bacterial infections and had a safety profile that we believe supports the further development of SPR206. The Phase 1 clinical trial of SPR206 was designed as a double-blind, placebo-controlled, ascending dose, multi-cohort study in healthy subjects. In this SAD and MAD Phase 1 clinical trial, a total of 96 healthy volunteers were randomized to receive SPR206 or placebo. All reported adverse events were mild to moderate and there were no reported severe or serious adverse events. No evidence of nephrotoxicity was observed and there were no subjects with clinically significant changes in laboratory tests during the study. SPR206 was well-tolerated at doses up to 100 mg administered three-times a day, a total of 300 mg daily, for 14 consecutive days. Pharmacokinetic data across the cohorts indicate dose linearity and dose proportionality as well as mean plasma drug exposures of SPR206 that are concordant with preclinical models predictive for clinical efficacy against target Gram-negative pathogens.

In Vitro Activity of SPR206 against MDR Gram-Negative Bacteria

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



Our Strategy

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

- ***Advance our lead product candidate tebipenem HBr to regulatory approval.*** In September 2020, Spero announced positive data from the ADAPT-PO Phase 3 trial evaluating an all oral regimen of tebipenem HBr head-to-head versus an all IV regimen of ertapenem for the treatment of adults with cUTI, including AP. The ADAPT-PO trial achieved its primary objective, demonstrating that oral tebipenem HBr was statistically non-inferior to intravenous ertapenem in the treatment of patients with cUTI and patients with AP with respect to the primary endpoint of overall response at the TOC visit in the micro-ITT population. Overall response (combined clinical cure plus microbiological eradication) rates at TOC were 58.8% for oral tebipenem versus 61.6% for IV ertapenem (treatment difference, -3.3%; 95% confidence interval [CI]: -9.7, 3.2; -12.5% NI margin). Comparative safety and tolerability data from 1,372 hospitalized adult patients enrolled in the study were similar between the tebipenem HBr and ertapenem treatment groups. We intend to make an NDA submission to the FDA for tebipenem HBr in the second half of 2021. In addition to cUTI, we believe that tebipenem HBr has the potential to treat other serious and life-threatening infections, including CABP. In December 2020, we initiated a Phase 1 bronchoalveolar lavage, or BAL, clinical trial to assess the penetration of tebipenem HBr into the pulmonary compartment and we expect to report data from the trial in second half of 2021. In addition, our tebipenem HBr collaboration with BARDA, which is further described elsewhere in this “Business” section of our Annual Report on Form 10-K, provides funding for a clinical trial in pneumonia patients.
- ***Establish global commercialization and marketing capabilities***. We have global commercialization rights to all of our product candidates, with the exception of tebipenem HBr and SPR206 in certain contractually specified Asian countries. Additionally, the Bill & Melinda Gates Medical Research Institute, or Gates MRI, holds rights to develop SPR720 for the treatment of lung infections caused by Mycobacterium tuberculosis in certain countries. Our management team has significant expertise in the commercialization of infectious disease treatments. Prior to joining us, members of our management team have collectively played leading roles in the approval and launch of 11 infectious disease products. We intend to build a targeted sales force and directly commercialize our product candidates in the United States in both hospital and community settings. Outside the United States, we intend to enter into collaborations with third parties to develop and market our product candidates in targeted geographical markets. By collaborating with companies that have an existing commercial presence and experience in such markets, we believe we can efficiently maximize the commercial potential of our product candidates.
- ***Diversify into rare orphan infectious disease markets such as NTM disease.*** We believe there is a significant opportunity to develop products for underserved “orphan” infectious disease areas, such as NTM disease. These markets offer the attributes of fewer branded or generic competitors as well as chronic therapy. We believe our drug candidate SPR720 has the potential to be the first oral antibiotic approved for the treatment of nontuberculous mycobacterial pulmonary disease. We may seek to acquire other product candidates for other underserved, debilitating orphan infectious diseases. We will evaluate our ability to continue to advance SPR720 through clinical development. In December 2020, we initiated a Phase 2a clinical trial of SPR720 in treatment inexperienced patients with NTM pulmonary disease due to MAC. On February 5, 2021, we announced that the FDA informed us that a clinical hold had been placed on our Phase 2a clinical trial of SPR720, which is further described elsewhere in this “Business” section of our Annual Report on Form 10-K under the heading “Update on Phase 2a Clinical Trial.” In December 2019, we reported Phase 1 data for SPR720 showing that SPR720 was generally well-tolerated, with a pharmacokinetic profile that we believe supports further development of the compound as an oral agent for the treatment of NTM disease. In June 2019, SPR720 was the focus of an equity investment by the Novo REPAIR Impact Fund for $10 million as well as a collaboration with Bill & Melinda Gates Medical Research Institute, or Gates MRI, to further the development of SPR720 for TB. In March 2020, the FDA granted orphan drug designation for SPR720 for the treatment of NTM infection, a designation available to drugs intended to treat a rare disease or condition that affects fewer than 200,000 persons in the United States. An orphan drug designation can provide specific benefits such as seven years of market exclusivity in the United States upon regulatory approval. In September 2020, SPR720 was awarded Fast Track Designation by the FDA for treatment of adult patients with NTM pulmonary disease.
- ***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 pipeline.*** We believe it may be beneficial to develop and commercialize one or more of our product candidates through partnering opportunities. Such collaborations may include regional collaborations to advance our pipeline products, 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.
- ***Continue to pursue collaborations with non-commercial organizations for scientific expertise and funding support.*** We have received funding support from BARDA, the United States National Institute of Allergy and Infectious Diseases, or NIAID, the United States 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 United States 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.

Collaboration, License and Service Agreements

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

Meiji Agreements

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

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

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

Under the Meiji License, we have paid Meiji a one-time nonrefundable upfront fee of $0.6 million and are obligated to pay Meiji future clinical and regulatory milestone payments up to an aggregate of $2.0 million and royalties of a low single-digit percentage based on net sales of tebipenem HBr. In October 2017, we paid a $1.0 million milestone payment to Meiji upon the enrollment of the first patient in our Phase 1 clinical trial of tebipenem HBr. Additionally, we are obligated to pay Meiji a percentage of certain amounts received from any sublicensees, up to an aggregate of $7.5 million.

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

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

IV Potentiator Product Agreements

Northern License Agreement

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

Cantab Agreements

In June 2016, we entered into a stock purchase agreement, or the Cantab Agreement, with Pro Bono Bio PLC, a corporation organized under the laws of England, and its affiliates, including PBB Distributions Limited, or PBB, Cantab Anti-Infectives Ltd., or CAI and New Pharma License Holdings Limited, or NPLH, in order to acquire NPLH and its intellectual property rights and assets relating to our Potentiator products, 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 ($6.8 million as of December 31, 2020) upon the achievement of a specified commercial milestone. We also agreed to pay royalties of a low single-digit percentage based on net sales of products licensed under the agreement. In addition, Spero Cantab issued an equity interest in Spero Cantab and entered into a subscription agreement and shareholders agreement with PBB. In July 2017, we repurchased PBB's minority equity interest in Spero Cantab in exchange for a one-time nonrefundable upfront fee of approximately $0.2 million and we also amended the Cantab Agreement to increase the contingent milestone payments to PBB by an aggregate of $0.1 million. The Cantab Agreement continues indefinitely, with royalty payment obligations thereunder continuing on a product-by-product and country-by-country basis until the later of ten years after the first commercial sale of such product in such country or the expiration in such country of the last to expire valid claim of any of the applicable patents.

In addition, we hold a NIAID contract that partially funded the next-generation potentiating agent development program. That contract was novated from CAI to us in December 2017. Under the contract we were obligated to pay PBB a percentage of funds received from NIAID up to a maximum of $1.3 million, which was fulfilled as of December 31, 2020.

Everest Medicines License Agreement

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

Under the terms of the Original Everest License Agreement, we received an upfront payment of $3.0 million. We also received a milestone payment of $2.0 million in the fourth quarter of 2020 upon completion and delivery of the results of a clinical study.

In January 2021, we entered into an amended and restated license agreement, or the Amended Everest License Agreement, with Everest and Potentiator, which amended and restated in its entirety the Original Everest License Agreement. The Amended Everest License Agreement modified the dates and values of certain milestone events related to development and commercialization of SPR206. Everest will now be making more significant investments in the development of SPR206 beyond what was contemplated at the time of the Original Everest License Agreement. The Original Everest License Agreement provided that we could receive up to $59.5 million upon achievement of certain milestones. The Amended Everest License Agreement provides that we may receive up to $38.0 million upon achievement of certain milestones, of which $2.0 million has been received to date. In addition, under the Amended Everest License Agreement, the Company assigned patents in the Territory to Everest, rather than licensing such patents to Everest, and the option related to SPR741 and related provisions have been removed. We are also entitled to receive high single-digit to low double-digit royalties on net sales, if any, of Licensed Products in the Territory following regulatory approval of SPR206. Everest has the right to sublicense to affiliates and third parties in the Territory.

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

Unless earlier terminated due to certain material breaches of the contract, or otherwise, the Amended 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 Amended Everest License Agreement may be terminated in its entirety by Everest upon 90 or 180 days' prior written notice, depending on the stage of development of the initial Licensed Product.

Other License, Collaboration and Service Agreements

Gates MRI Collaboration

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

Vertex Assignment and License Agreement

In May 2016, we entered into an agreement with Vertex Pharmaceuticals Incorporated, or Vertex, pursuant to which Vertex assigned to us rights to patents relating to SPR720 and SPR719 (an active metabolite). The acquired patent portfolio includes protection for composition of matter, method of use, and specific key intermediates used in the manufacture of SPR719 and SPR720. We also obtained certain know-how and a license to research, develop, manufacture and sell products for a proprietary compound, as well as a transfer of materials as part of the transaction. In return, we granted Vertex an exclusive license to the assigned patents and know-how for use outside of the diagnosis, treatment or prevention of bacterial infections. In exchange for the assigned patents, we paid Vertex an upfront, one-time, non-refundable, non-creditable fee of $0.5 million, which was recognized as research and development expense, and we also agreed to pay Vertex future clinical, regulatory and commercial milestones up to $81.3 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 year ended December 31, 2020, we paid and recorded $0.9 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.

Savior Service Agreement

In November 2018, we entered into a service agreement with Savior Lifetec Corporation, or Savior, to perform technology transfer, process development, analytical method development and testing and formulation development for tebipenem HBr. Per the terms of the agreement, we paid Savior a non-refundable supervision fee of approximately $2.0 million to manage the buildout of a commercial manufacturing facility. The supervision fee is classified as a prepaid asset on our balance sheet and is being amortized over a service period of approximately 34 months. We have paid Savior an additional $5.1 million for facility build out costs, which is classified as a long-term asset on our balance sheet as of December 31, 2020.

Government Awards

Through December 31, 2020, we have committed funding support of up to an aggregate of $49.7 million in non-dilutive funding from BARDA, NIAID, the DoD and concluded awards from CARB-X, SBIR and the DoD, with the potential to receive a total of up to $63.0 million (inclusive of amounts we have already received) if certain options are exercised. The awards are subject to termination for convenience at any time by the granting government agency, and the granting government agency is not obligated to provide funding to us beyond the base period amounts from Congressionally approved annual appropriations. These awards are structured in the following manner:

- BARDA award to support the further clinical development of tebipenem HBr. The BARDA award provides total reimbursement to us of up to $46.8 million for qualified expenses for tebipenem HBr development over a five-year period. The award initially committed funding of $15.7 million over a three-year base period from July 2018 to June 30, 2021 for cUTI development activities. In May 2019, the contract was modified to include additional funding of approximately $2.5 million for tebipenem HBr, increasing the amount of initial committed funding from $15.7 million to approximately $18.2 million. In January 2020, BARDA exercised its first option under the contract, committing $15.9 million for tebipenem HBr through November 2021. Total committed funding under the BARDA award to date is $34.1 million, including the first option exercised in 2020. There is a second option exercisable by BARDA for the remaining $12.7 million of funding, subject to specified milestones being achieved under the award agreement. As part of our tebipenem HBr collaboration with BARDA described above, there will be studies assessing the efficacy of tebipenem HBr in treatment of infections caused by biodefense threats such as anthrax, plague, and melioidosis, including a clinical trial in pneumonia patients. The Defense Threat Reduction Agency, or DTRA, will provide up to $10.0 million in addition to the total potential $46.8 million from BARDA, to cover the cost of the nonclinical biodefense aspects of the collaboration program. While such funding would be for the purpose of developing tebipenem HBr in these areas, we will not receive any funds directly from DTRA. Upon these achievements, BARDA may exercise its second option to fund a clinical trial in pneumonia patients to demonstrate safety and data suggestive of efficacy.
- NIAID funding for SPR206. The NIAID contract for SPR206 provides for total development funding of up to $6.5 million over a base period and three option periods. To date, funding for the base period and the first two option periods, totaling $5.9 million, have been committed through March 2021.
- NIAID award under its Small Business Innovation Research program, or SBIR, for SPR720. This award provided up to $1.0 million of support for our SPR720 program. The scope of the program included *in vitro* and *in vivo* assessments of SPR720 against TB as well as nonclinical and manufacturing activities in support of both TB and NTM indications. The NIAID SBIR award was structured as a base period followed by a single option. For the base period of March 1, 2017 through February 28, 2018, NIAID committed funding of approximately $0.6 million for the SPR720 program. In February 2018 NIAID exercised the approximately $0.4 million option, with a period of performance from March 1, 2018 through February 28, 2019. In January 2019, the period of performance for this award was extended through February 28, 2020. This award has been closed out as of December 31, 2020.
- DoD funding for SPR206. In July 2019 we were awarded a $5.9 million award from the DoD Congressionally Directed Medical Research Programs, or CDMRP, Joint Warfighter Medical Research Program, which will support, over a four-year period into July 2023, the development of SPR206. The funding will cover the costs of select Phase 1 pharmacology studies, a 28-day GLP non-human primate toxicology study, and microbiological surveillance studies that would be required for a potential NDA submission with the FDA for SPR206. This award was preceded by a DoD cooperative agreement award made to Spero in September 2016 that funded our potentiator product candidates to develop anti-infective agents to combat Gram-negative bacteria. It was structured as a single, two-year $1.5 million award with a period of performance through September 2019. That award has now been closed out.

Intellectual Property

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

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

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

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

Tebipenem HBr Oral Carbapenem (Tebipenem Pivoxil Hydrobromide)

Our tebipenem HBr program contains two pending United States provisional patent applications, one issued and two pending United States patent applications, and four issued and 37 pending foreign patent applications covering novel preparations of tebipenem pivoxil hydrobromide as of December 31, 2020, all wholly owned by us. The provisional patent application must be converted to PCT applications within one year of their May 2020 and November 2020 filing dates. The issued foreign patents are issued in Australia (2), Brazil, and South Africa. Foreign patent applications are pending in Australia, Brazil, Canada, China, Colombia, the Eurasian Patent Office, the European Patent Office, Egypt, Indonesia, Israel, India, Japan, South Korea, Mexico, New Zealand, the Philippines, Singapore, Thailand, Vietnam, and South Africa. United States and foreign patents covering our tebipenem pivoxil hydrobromide preparations will have statutory expiration dates of December 2037, February 2038, May 2040, and November 2040. Patent term adjustments or patent term extensions could result in later expiration dates.

In January 2021, the United States Patent and Trademark Office, or USPTO, issued U.S. Patent No, 10,889,587, which is directed to the crystalline formulation of tebipenem HBr, Spero's oral carbapenem in development for the treatment of cUTI and AP. This patent covers a crystalline form of tebipenem pivoxil HBr, pharmaceutical compositions of tebipenem pivoxil HBr and methods of use. The patent expires in February 2038.

Next-Generation Potentiator Product (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, 2020, we owned one United States patent and three pending United States patent applications, ten foreign patents, and 46 pending foreign patent applications in a number of jurisdictions including Argentina, Australia, Brazil, Canada, China, Colombia, the Eurasian Patent Office, the European Patent Office, Hong Kong, India, Israel, Japan, South Korea, Malaysia, Mexico, New Zealand, the Philippines, Russia, Singapore, South Africa, Taiwan, Thailand, Ukraine, Venezuela and Vietnam. Issued United States or foreign patents and any patents issuing from pending United States or foreign applications covering our next-generation polymyxin program will have a statutory expiration date of May 2034, March 2035, November 2035, or June 2039. Patent term adjustments or patent term extensions could result in later expiration dates.

In 2019 Spero entered into an agreement with Everest, by which Everest would develop, manufacture, and commercialize SPR206 in China, South Korea, and certain Southeast Asian countries. Spero's agreement with Everest has since been amended to include an obligation by Spero to assign its SPR206 patent rights to Everest in these countries.

NTM Disease Program (SPR720)

Our intellectual property portfolio for our DNA Gyrase Inhibitor program includes issued patents and pending patent applications directed to composition of matter for SPR720, and its close analogs and prodrugs, novel solid forms of SPR720 and its prodrugs, methods of manufacture, and methods of treatment using SPR720 alone and in combination with other antibiotic compounds. All patents and patent applications in the portfolio are wholly owned by us. As of December 31, 2020, we owned 11 issued United States patents, 91 issued foreign patents, and seven 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 United States and foreign patents, and patents issuing from pending United States 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 USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug, 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 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, and human resources than we do, as well as greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our potential competitors may be more successful than us in obtaining FDA approval of 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 our most advanced product candidate, tebipenem HBr, if approved, will be efficacy, coverage of drug-resistant strains of bacteria, safety and tolerability profile, reliability, convenience of oral dosing, price, availability of reimbursement from governmental and other third-party payers and susceptibility to drug resistance.

We are developing tebipenem HBr as an oral antibiotic for use as a monotherapy for the treatment of resistant and MDR infections. If approved, tebipenem HBr would compete with several antibiotics currently in clinical development for urinary tract infection, including sulopenem from Iterum Therapeutics Limited, ARX-1796 from Pfizer, Gepotidacin from GSK and Pivmecillinam from Utilility Therapeutics. We also expect that tebipenem HBr, if approved, would compete with future and current generic versions of marketed antibiotics. If approved, we believe that tebipenem HBr would compete effectively against these compounds on the basis of tebipenem HBr's potential:

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

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

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

Government Regulation and Product Approval

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

United States 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 United States 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 GLPs and other applicable 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 GCPs to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA and payment of user fees;
- 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 cGMPs, 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
- 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. A clinical hold may occur at any time during the life of an IND and may affect one or more specific studies or all studies conducted under the IND.

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 and clinical trial results must be submitted within specific timeframes to the National Institutes of Health, or 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 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. Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by a significant user fee. The FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual program fee for prescription drug products. Fee waivers or reductions are available in certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation, or where the applicant is a small business submitting its first human therapeutic application for review.

Under the performance goals and policies agreed to by the FDA under PDUFA, 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, and six months from the filing date for an application with priority review. This review typically takes 12 months from the date the NDA is submitted to FDA (eight months for priority applications) 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 (or six months for priority applications) 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.

During the review and approval process, the FDA likely will re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan if it determines that a REMS is necessary to ensure that the benefits of the drug outweigh its risks and to assure the safe use of the drug. 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 or a drug that presents difficult questions of safety or efficacy 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 that the clinical trials were conducted in compliance with IND regulations and GCP requirements and to assure the integrity of the clinical data submitted to the FDA.

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 United States population and United States 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 a new drug product 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. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A complete response letter, or CRL, describes all of the specific deficiencies in the NDA identified by the agency. A CRL indicates that the review cycle of the application is complete and the application will not be approved in its present form. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the CRL may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter to the applicant. The FDA has committed to reviewing such resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

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 plan, 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

The FDA is authorized to designate certain products for expedited development or review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include fast track designation, breakthrough therapy designation, QIDP designation, and priority review designation. 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. In addition, fast track designation may be withdrawn by the sponsor or rescinded by the FDA if the designation is no longer supported by data emerging in the clinical trial process. Tebipenem HBr has been granted fast track designation by the FDA for the treatment of cUTI and AP, and in September 2020, SPR720 received fast track designation for treatment of adult patients with NTM pulmonary disease.

In addition, with the enactment of the FDA Safety and Innovation Act, or FDASIA, in 2012, Congress created a new regulatory program for therapeutic candidates designated by FDA as "breakthrough therapies" upon a request made by the IND sponsors. 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. The FDA must take certain actions with respect to breakthrough therapies, such as holding timely meetings with and providing advice to the product sponsor, intended to expedite the development and review of an application for approval of a breakthrough therapy.

FDASIA also included the Generating Antibiotics Incentives Now Act, or the GAIN Act, which directed the FDA to implement the qualified infectious disease product, or QIDP, designation program. The GAIN Act created incentives for the development of antibacterial and antifungal drug products for the treatment of serious or life-threatening infections. A therapeutic candidate designated as a QIDP is eligible for fast track designation, and the first marketing application submitted for a specific drug product and indication for which QIDP designation was granted will be granted priority review. A subsequent application from the same sponsor for the same product and indication will receive priority review designation only if it otherwise meets the criteria for priority review. As discussed further below under "Qualified Infectious Disease Product Exclusivity," the GAIN Act also provides the possibility of a five-year exclusivity extension that is added to any other marketing exclusivity for which a QIDP-designated drug qualifies upon FDA approval.

Finally, the FDA may designate a product for priority review if it is a drug or biologic that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines at the time that the marketing application is submitted, on a case-by-case basis, whether the proposed drug represents a significant improvement in treatment, prevention or diagnosis of disease when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months for an NDA for a new molecular entity from the date of filing.

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. Furthermore, fast track designation, breakthrough therapy designation and priority review do not change the standards for approval and may not ultimately expedite the development or approval process.

Accelerated Approval Pathway

In addition, a product studied for its 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, or IMM, and that is reasonably likely to predict an effect on IMM 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 IMM or other clinical endpoint, and the drug may be subject to expedited withdrawal procedures. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a therapeutic candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm the predicted clinical benefit of the product during post-marketing studies, would allow the FDA to withdraw approval of the drug. All promotional materials for drug products being considered and approved under the accelerated approval program are subject to prior review by the FDA.

Limited Population Antibacterial Drug Pathway

On December 13, 2016, former President Obama signed into law the Cures Act, which is intended to accelerate medical product development. Section 3042 of the Cures Act established 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. To date, the FDA has approved two products under this pathway, and in August 2020 it published a final guidance for industry entitled "Limited Population Pathway for Antibacterial and Antifungal Drugs" that describes the criteria, processes, and other general considerations for demonstrating the safety and effectiveness of limited population antibacterial and antifungal drugs, or LPADs, and is intended to assist sponsors in their development of certain new products for approval under the LPAD pathway.

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. Certain modifications to the product, including changes in indications or manufacturing processes or facilities, may require the applicant to develop additional data or conduct additional preclinical studies and clinical trials to support the submission to FDA. There also are continuing, annual user fee requirements for any marketed products, 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, FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. 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 and other laws. Changes to the manufacturing process are strictly regulated and, depending on the significance of the change, may 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 compliance with cGMP and other aspects of quality control and quality assurance.

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 and for use in patient populations described in the product's approved labeling. Promotional claims must also be consistent with the product's FDA-approved label, including claims related to safety and effectiveness. The government also closely scrutinizes the promotion of prescription drugs in specific contexts such as direct-to-consumer advertising, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. After 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 clinical holds on post-approval clinical trials;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; or
- consent decrees, corporate integrity agreements, debarment, or exclusion from federal health care programs.

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. Most recently, the Drug Supply Chain Security Act, or the DSCSA, was enacted with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that is expected to culminate in November 2023.

Regulatory Exclusivity and Approval of Follow-on Products

Hatch-Waxman Exclusivity

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress enacted Section 505(b)(2) of the FDCA and also established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are “abbreviated” because they cannot include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer must rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is “bioequivalent” to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if “the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug.”

Upon approval of an ANDA, the FDA indicates whether the generic product is “therapeutically equivalent” to the RLD in its publication “Approved Drug Products with Therapeutic Equivalence Evaluations,” also referred to as the “Orange Book.” Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA’s designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

In contrast, Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. A Section 505(b)(2) applicant may eliminate the need to conduct certain preclinical or clinical studies if it can establish that reliance on studies conducted for a previously-approved product is scientifically appropriate. Unlike the ANDA pathway used by developers of bioequivalent versions of innovator drugs, which does not allow applicants to submit new clinical data other than bioavailability or bioequivalence data, the 505(b)(2) regulatory pathway does not preclude the possibility that a follow-on applicant would need to conduct additional clinical trials or nonclinical studies; for example, it may be seeking approval to market a previously approved drug for new indications or for a new patient population that would require new clinical data to demonstrate safety or effectiveness.

As part of the NDA review and approval process, applicants are required to list with the FDA each patent that has claims that cover the applicant's product or method of therapeutic use. Upon approval of a new drug, each of the patents listed in the application for the drug is then published in the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential follow-on competitors in support of approval of an ANDA or 505(b)(2) NDA.

When an ANDA applicant submits its application to the FDA, it is required to certify to the FDA concerning any patents listed for the reference product in the FDA's Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. Moreover, to the extent that the Section 505(b)(2) NDA applicant is relying on studies conducted for an already approved product, the applicant also is required to certify to the FDA concerning any patents listed for the NDA-approved product in the Orange Book to the same extent that an ANDA applicant would.

If the follow-on applicant does not challenge the innovator's listed patents, the FDA will not approve the ANDA or 505(b)(2) application until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the follow-on applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) NDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA/505(b)(2) applicant.

An ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivities listed in the Orange Book for the referenced product have expired. The Hatch-Waxman Amendments to the FDCA provided 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, or NCE. For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA or 505(b)(2) NDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of data exclusivity if an NDA or NDA supplement includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as new indications, dosage forms, route of administration or combination of ingredients. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs or 505(b)(2) NDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; rather, 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 follow-on applications for drugs containing the original active ingredient.

Five-year and three-year exclusivity also will not delay the submission or approval of a traditional NDA filed under Section 505(b)(1) of the FDCA; however, an applicant submitting a traditional NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. For drug products that contain an "antibiotic" ingredient approved prior to 1997, the statute imposes certain limitations on the award of non-patent exclusivity. However, we do not believe these limitations would apply to tebipenem HBr or any of our other investigational antibiotics currently in preclinical and clinical development.

Qualified Infectious Disease Product Exclusivity

Under the GAIN Act, the FDA may designate a product as a QIDP. In order to qualify for designation as a QIDP, the drug product candidate must be 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. We obtained a QIDP designation for the oral formulation of tebipenem HBr for cUTI in November 2016 and CABP and DFI in April 2017. We were granted QIDP designation by the FDA for SPR206 in October 2018 for the treatment of cUTI and hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP). In February 2019, 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*.

In addition to the expedited review benefits for which a QIDP-designated drug candidate may be eligible, such a drug that is approved for the use for which the QIDP designation was granted will receive a five-year extension to any non-patent marketing exclusivity period for which the drug qualified upon approval, such as five-year NCE exclusivity, three-year new clinical data exclusivity, seven-year orphan exclusivity, or six-month pediatric exclusivity. This so-called GAIN exclusivity extension is not available to a QIDP-designated drug that has previously received the five-year extension period, such as when an applicant is seeking approval for a new indication or new strength.

Orphan Drug Designation and Exclusivity

In March 2020, the FDA granted orphan drug designation for SPR720 for the treatment of NTM infection. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects either (i) fewer than 200,000 individuals in the United States, or (ii) more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Legislative proposals are currently being considered that would revise or revoke the second option available for a drug candidate to receive an orphan designation, the so-called "cost recovery" pathway. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use will be disclosed publicly by the FDA; the posting will also indicate whether a drug is no longer designated as an orphan drug.

More than one product candidate may receive an orphan drug designation for the same indication, and the same product candidate can be designated for more than one qualified orphan indication. The benefits of orphan drug designation include research and development tax credits and exemption from FDA prescription drug user fees. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process if or when an NDA for the drug candidate is filed.

If a product that has orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan product exclusivity, which means that for seven years, the FDA may not approve any other marketing applications for the same drug for the same indication, except under limited circumstances described further below. Orphan exclusivity does not block the approval of a different drug for the same rare disease or condition, nor does it block the approval of the same drug for different conditions. As a result, even if one of our product candidates receives orphan drug exclusivity, the FDA can still approve different drugs for use in treating the same indication or disease, which could create a more competitive market for our drug products, if approved for marketing in the future. Additionally, if a drug designated as an orphan product receives marketing approval for an indication broader than what was designated, it may not be entitled to orphan drug exclusivity.

Orphan exclusivity will not bar approval of another product with the same drug for the same condition under certain circumstances, including if a subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety or a major contribution to patient care, or if the company with orphan drug exclusivity cannot assure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated. Following amendments made to the statute as part the FDA Reauthorization Act of 2017, the FDA is required to publish a summary of the clinical superiority findings when a drug is eligible for orphan product exclusivity on the basis of a demonstration of clinical superiority.

In addition, the FDA finalized guidance in 2018 indicating that it does not expect to grant any additional orphan drug designation to products for pediatric subpopulations of common diseases. Nevertheless, FDA intends to still grant orphan drug designation to a drug that otherwise meets all other criteria for designation when it prevents, diagnoses or treats either (i) a rare disease that includes a rare pediatric subpopulation, (ii) a pediatric subpopulation that constitutes a valid orphan subset, or (iii) a rare disease that is in fact a different disease in the pediatric population as compared to the adult population.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity available in the United States and, if granted, it provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity or listed patents. Under the Best Pharmaceuticals for Children Act, or BPCA, certain therapeutic candidates may obtain an additional six months of exclusivity if the sponsor submits information requested in writing by the FDA, referred to as a Written Request, relating to the use of the active moiety of the product candidate in children. The data do not need to show the product to be effective in the pediatric population studied; rather, the additional protection is granted if the pediatric clinical trial is deemed to have fairly responded to the FDA's Written Request. Although the FDA may issue a Written Request for studies on either approved or unapproved indications, it may only do so where it determines that information relating to that use of a product candidate in a pediatric population, or part of the pediatric population, may produce health benefits in that population. The issuance of a Written Request does not require the sponsor to undertake the described trials. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

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, or EU, 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 underwent a major change when the Clinical Trial Regulation became effective, which initially had been scheduled to occur in 2019 but has been delayed. 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 EU Member States and the European Commission.

In June 2016, the electorate in the United Kingdom. voted in favor of leaving the EU (commonly referred to as "Brexit"). Thereafter, in March 2017, the country formally notified the EU of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty, and the United Kingdom formally left the EU on January 31, 2020. A transition period began on February 1, 2020, during which EU pharmaceutical law remained applicable to the United Kingdom. This transition period ended on December 31, 2020. Since the regulatory framework in the United Kingdom covering the quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of medicinal products is derived from EU Directives and Regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom, as United Kingdom legislation now has the potential to diverge from EU legislation. It remains to be seen how Brexit will impact the regulatory regime in the United Kingdom in the long-term. The Medicines and Healthcare products Regulatory Agency has recently published detailed guidance for industry and organizations to follow from January 1, 2021 now the transition period is over, which will be updated as the United Kingdom's regulatory position on medicinal products evolves over time.

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 EU Member States, with EMA managing the database and supervising content publication on the public website.

Under EU 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 EMA 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 EU 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, Pricing and Reimbursement

Sales of our products, if approved for marketing, 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. There may be significant delays in obtaining coverage and reimbursement for approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or regulatory authorities in other countries. It is time consuming and expensive to seek reimbursement from third-party payors. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower cost products that are already reimbursed and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by third-party payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. In the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but they also have their own methods and approval process apart from Medicare coverage and reimbursement determinations. Accordingly, one third-party payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product.

In addition, 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 United States 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. Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Individual states in the United States have also increasingly passed legislation and implemented 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. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers, or PBMs, and other members of the health care and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area.

In the United States, the federal government provides health insurance for people who are 65 years 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 United States 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, or DHHS, 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. As another example, the 2021 Consolidated Appropriations Act signed into law on December 27, 2020 incorporated extensive healthcare provisions and amendments to existing laws, including a requirement that all manufacturers of drug products covered under Medicare Part B report the product's average sales price, or ASP, to DHHS beginning on January 1, 2022, subject to enforcement via civil money penalties.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA and as a result certain sections of the ACA have not been fully implemented or effectively repealed. Members of Congress have indicated that they may continue to seek to modify, repeal or otherwise invalidate all, or certain provisions of, the ACA. For example, the Tax Cuts and Jobs Act, or TCJA, was enacted in 2017 and, among other things, removed penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance, commonly referred to as the "individual mandate." In December 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate was a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the TCJA, the remaining provisions of the ACA were invalid and the law in its entirety was unconstitutional. In December 2019, the U.S. Court of Appeals for the Fifth Circuit upheld the District Court ruling that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether other reforms enacted as part of the ACA but not specifically related to the individual mandate or health insurance could be severed from the rest of the ACA so as not to be declared invalid as well. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case and allocated one hour for oral arguments, which occurred on November 10, 2020. A decision from the Supreme Court is expected to be issued in mid-2021. 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 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 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 when adopting decisions concerning the pricing and reimbursement of a specific medicinal product.

Other Healthcare Laws

Our current and future business operations are subject to healthcare regulation and enforcement by the federal government and the state and foreign governments where we research, and, if approved, market, sell and distribute our therapeutic candidates. These laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security, physician sunshine and drug pricing transparency laws and regulations such as:

- The federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. The federal Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the federal Anti-Kickback Statute to reach large settlements with healthcare companies based on sham consulting and other financial arrangements with physicians. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- The federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalty laws, prohibit, among other things, knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the U.S. government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. government. Actions under these laws may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. The federal government uses these laws, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the U.S., for example, in connection with the promotion of products for unapproved uses and other allegedly unlawful sales and marketing practices;
- The U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal, civil and criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- The Physician Payments Sunshine Act, enacted as part of the ACA, among other things, imposes reporting requirements on manufacturers of FDA-approved drugs, devices, biologics and medical supplies covered by Medicare or Medicaid to report, on an annual basis, to DHHS information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, chiropractors and, beginning in 2022 for payments and other transfers of value provided in the previous year, certain advanced non-physician health care practitioners), teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations impose specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities, which include certain healthcare providers, health plans, and healthcare clearinghouses, that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions; and

- Analogous state laws and regulations, such as state anti-kickback and false claims laws which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state laws which require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug and therapeutic biologics manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and pricing information; state and local laws which require the registration of pharmaceutical sales representatives; and state laws and non-United States laws and regulations that govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect the ability to profitably sell product candidates that obtain marketing approval. The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our current or future product candidates. For example, in August 2017, the FDA Reauthorization Act was signed into law, which reauthorized the FDA's user fee programs and included additional drug and device amendments to the FDCA, and in December 2019, former President Trump signed into law the Creating and Restoring Equal Access to Equivalent Samples Act or the "CREATES Act," which aims to address the concern articulated by both the FDA and others in the industry that some reference product manufacturers have improperly restricted the distribution of their products, including by invoking the existence of a REMS for certain products, to deny generic product developers access to samples of brand products. The CREATES Act established a private cause of action that permits a generic product developer to sue the reference product manufacturer to compel it to furnish the necessary samples on "commercially reasonable, market-based terms." Whether and how generic product developers will use this new pathway, as well as the likely outcome of any legal challenges to provisions of the CREATES Act, remain highly uncertain and its potential effects on our future commercial products are unknown.

As another example, in November 2020 the Trump Administration finalized regulations aimed at implementing a system whereby state governmental entities could lawfully import and distribute prescription drugs sourced from Canada, with the stated goal of lowering drug prices domestically. However, the impact of such future programs is uncertain, in part because lawsuits have been filed challenging the government's authority to promulgate these regulations, but also because they may be vulnerable to being overturned by a joint resolution of disapproval from Congress under the procedures set forth in the Congressional Review Act, which could be applied to regulatory actions taken by the Trump Administration on or after August 21, 2020 (*i.e.*, in the last 60 days of legislative session of the 116th Congress). Other regulatory actions that were initiated or finalized during the final months of the Trump Administration are also subject to uncertainty following the January 20, 2021 transition to a new Democrat-led presidential administration. Following his inauguration, President Biden took immediate steps to order a regulatory freeze on all pending substantive executive actions in order to permit incoming department and agency heads to review whether questions of fact, policy, and law may be implicated and to determine how to proceed.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we otherwise may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations. Moreover, among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access.

Manufacturing

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

Human Capital

As of December 31, 2020, we had 89 full-time employees, including a total of 20 employees with M.D. or Ph.D. degrees. Of these employees, 55 employees were primarily engaged in research and development activities, and 34 provide administrative, business and operations support. All of these employees were based in the United States. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our employee relations to be good.

We hire and maintain an experienced, committed, diverse, inclusive and highly motivated workforce. Effective attraction, development, and retention of human resource talent, or human capital, is vital to the success of our mission-driven growth strategy. We face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions, and we believe that our future success will depend in large part on our continued ability to attract and retain highly skilled employees. To attract qualified applicants to our company and retain our employees, we offer a competitive rewards package consisting of base salary and cash target bonus, a comprehensive benefit package and equity compensation.

We want our employees to learn, grow and look for ways to help develop skills through industry, company and functional training, as well as mentoring opportunities. We offer a robust set of career-enhancing learning experiences and initiatives to all employees, aligned with our mission, vision, and values.

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 United States 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 securities 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 actually occurs, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected, and the trading price of our securities 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 the COVID-19 Pandemic

The outbreak of the novel strain of coronavirus, SARS-CoV-2, which causes COVID-19, could adversely impact our business, including our preclinical studies and clinical trials.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. In December 2019, a novel strain of coronavirus, SARS-CoV-2, which causes coronavirus disease 2019 (COVID-19), surfaced in Wuhan, China. Since then, COVID-19 has spread globally. In response to the spread of COVID-19, we have closed our offices with our administrative employees continuing their work outside of our offices and restricted on-site staff to only those required to execute their job responsibilities.

As a result of the COVID-19 outbreak, or similar pandemics, we have experienced, and may in the future experience, certain disruptions that could materially impact our business, preclinical studies and clinical trials. Such disruptions may include:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays or disruptions in preclinical studies or clinical trials due to unforeseen circumstances at contract research organizations and vendors along their supply chain;

- increased rates of patients withdrawing from our clinical trials following enrollment as a result of contracting COVID-19, being forced to quarantine, or not being willing to travel to clinical trial sites;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring and data collection, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (particularly any procedures that may be deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies, which may impact approval timelines and other agency interactions;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems; and
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families, the desire of employees to avoid contact with large groups of people, continued reliance on working from home or mass transit disruptions.

These and other factors arising from the COVID-19 pandemic could worsen in countries that are already afflicted with COVID-19 or could return to countries where the pandemic has been partially contained, each of which could further adversely impact our ability to conduct clinical trials and our business generally, and could have a material adverse impact on our business, operations and financial condition and results.

In addition, the trading prices for our common stock and the securities of other biopharmaceutical companies have been highly volatile. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms. The COVID-19 outbreak continues to evolve rapidly. The extent to which the outbreak may impact our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the outbreak, travel restrictions and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

Risks Related to Our Financial Position and Need for Additional Capital

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

We have not generated any revenue from the sale of our products and have incurred losses in each year since our inception in 2013. Our net losses were $78.3 million and $60.9 million during the years ended December 31, 2020 and 2019, respectively. All of our product candidates are in development, none have been approved for sale and we may never have a product candidate approved for commercialization.

In accordance with Accounting Standards Update, or ASU, 2014-15, Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern (Subtopic 205-40), we are required to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern from the issuance date of our financial statements. Based on our current plans, we believe that our existing cash, cash equivalents and marketable securities as of December 31, 2020, together with the committed funding from our existing BARDA contract and other non-dilutive funding commitments, will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2022, including through the submission of the NDA for tebipenem HBr. This timeline is subject to uncertainty as to the timing of future expenditures. We have developed plans to mitigate this risk, which primarily consist of raising additional capital through some combination of equity or debt financings, potential new collaborations, additional grant funding and/or reducing cash expenditures. If we are not able to secure adequate additional funding, we plan to make reductions in spending. In that event, we may have to delay, scale back, or eliminate some or all of our planned clinical trials, research stage programs and commercial activities. The actions necessary to reduce spending under this plan at a level that mitigates the factors described above is not considered probable, as defined in the accounting standards and therefore, the full extent to which management may extend our funds through these actions may not be considered in management’s assessment of our ability to continue as a going concern. As a result, we have concluded that substantial doubt exists about our ability to continue as a going concern.

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

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

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

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

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

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

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

We believe that our existing cash, cash equivalents and marketable securities as of December 31, 2020, together with the committed funding from our existing BARDA contract and other non-dilutive funding commitments will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2022, including through the submission of the NDA for tebipenem HBr. Our cash forecasts are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

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

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

For the year ended December 31, 2020, our non-dilutive sources of funding consisted of an award from BARDA for tebipenem HBr, an award from NIAID under its Small Business Innovation Research program or SBIR, for our SPR720 program, an award from NIAID for SPR206, an award from the DoD that provides partial funding for the development of our Potentiator product candidates and an award from the DoD Congressionally Directed Medical Research Programs, or CDMRP, Joint Warfighter Medical Research Program for SPR206.

The BARDA award provides total reimbursement to us of $46.8 million for qualified expenses for tebipenem HBr development over a five-year period through November 2021. The award initially committed funding of $15.7 million over a three-year base period from July 2018 to June 2021 for cUTI development activities. In May 2019, the contract was modified to include additional funding of approximately $2.5 million for tebipenem HBr, increasing the amount of initial committed funding from $15.7 million to approximately $18.2 million. In February 2020, BARDA exercised its first option under the contract, committing $15.9 million for tebipenem HBr through November 2021. Total committed funding under the BARDA award to date is $34.1 million, including the first option exercised in 2020. There is a second option exercisable by BARDA for the remaining $12.7 million of funding, subject to specified milestones being achieved under the award agreement. As part of our tebipenem HBr collaboration with BARDA described above, there will be studies assessing the efficacy of tebipenem HBr in treatment of infections caused by biodefense threats such as anthrax, plague, and melioidosis, including a clinical trial in pneumonia patients. The Defense Threat Reduction Agency, or DTRA, will provide up to $10.0 million in addition to the total potential $46.8 million from BARDA, to cover the cost of the nonclinical biodefense aspects of the collaboration program. While such funding would be for the purpose of developing tebipenem HBr in these areas, we will not receive any funds directly from DTRA. Upon these achievements, BARDA may exercise its second option to fund a Phase 2 clinical trial in community-acquired bacterial pneumonia patients to demonstrate safety and data suggestive of efficacy.

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

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

Unless and until we can generate a substantial amount of revenue from our product candidates, we expect to finance our future cash needs through public or private equity offerings, debt financings, collaborations, licensing arrangements and government funding arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. We are filing a universal shelf registration statement on Form S-3 with the SEC concurrently with the filing of this Annual Report on Form 10-K, which when declared effective, will register for sale up to $300.0 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 $75.0 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," or ATM, 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, 2020, we had United States federal, state and foreign net operating loss carryforwards, or NOLs, of $228.1 million, $226.2 million and $10.7 million, respectively. The federal NOLs of $73.0 million will expire at various dates from 2033 to 2037 and approximately $155.1 million can be carried forward indefinitely. The state NOLs begin to expire in 2033 and will expire at various dates through 2039. The foreign NOLs do not expire. Utilization of these NOLs depends on many factors, including our future income, which cannot be assured. These NOLs could expire unused and be unavailable to offset our future income tax liabilities. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership by 5% stockholders over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes to offset its post-change income may be limited. We have not determined if we have experienced Section 382 ownership changes in the past and if a portion of our NOLs is subject to an annual limitation under Section 382. In addition, we may experience ownership changes in the future as a result of subsequent changes in our stock ownership, some of which may be outside of our control. If we determine that an ownership change has occurred and our ability to use our historical NOLs is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

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

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

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

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

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

Risks Related to Product Development and Commercialization

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

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

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

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

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

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

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

If clinical trials of product candidates that we 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 such product candidates.

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

The clinical development of tebipenem HBr, SPR720 and any of our other product candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to demonstrate efficacy in a trial or across a broad population of patients, the occurrence of severe adverse events, failure to comply with protocols or applicable regulatory requirements, and determination by the FDA or any comparable foreign regulatory authority that a drug product is not approvable. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in clinical trials, even after promising results in earlier nonclinical studies or clinical trials. The results of preclinical and other nonclinical studies and/or early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Notwithstanding any promising results in early nonclinical studies or clinical trials, we cannot be certain that we will not face similar setbacks. For example, although tebipenem HBr is a new formulation of the active pharmaceutical ingredient tebipenem that exhibited a favorable safety and efficacy profile during clinical trials conducted by Meiji and a global pharmaceutical company, which we refer to as Global Pharma, in Japan, we may nonetheless fail to obtain regulatory approval for tebipenem HBr for the treatment of cUTI based on the results of our recently completed Phase 3 clinical trial and those supporting foreign data.

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

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

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

- the FDA or other comparable foreign regulatory authorities may disagree as to the design or implementation of our clinical trials;
- we may be delayed in or fail to reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, participants may drop out of these clinical trials at a higher rate than we anticipate or we may fail to recruit suitable patients to participate in clinical trials;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the FDA or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical trials of our product candidates for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we enter into agreements for clinical and commercial supplies;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the institutional review boards, or IRBs, of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, if any, for such trial or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug or changes in governmental regulations or administrative actions. On February 5, 2021, we announced that the FDA informed us that a clinical hold had been placed on our Phase 2a clinical trial of SPR720 following mortality events in a non-human primate toxicology study.

If we are required to conduct additional clinical trials or other testing of tebipenem HBr, SPR720 or any other product candidate beyond the trials and testing that we contemplate, if we are unable to successfully complete clinical trials or other testing of our product candidates, if the results of these trials or tests are unfavorable or are only modestly favorable or if there are safety concerns associated with tebipenem HBr or any other product candidate, we may:

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

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

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

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

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

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.

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

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

- The studies were not randomized and were open-label and had no comparator arm. Treatment assignments were made by the investigators;
- The inclusion criteria specified complicated UTI as an entry criterion, but other than retained residual volume (100 ml) there were no other criteria defining "complicated" UTI;
- While L-084 04 excluded patients who received prior antibiotics and who had no clinical response, there were no parameters or limits for inclusion (e.g., less than 24 hours of a potentially effective antibiotic or number of doses). ME1211 did not specifically mention prior antibiotic use;
- While urine cultures were obtained at baseline, these were not quantitative, and there was no minimum requirement for bacterial load for entry;

- While microbiological outcome was assessed, the definitions did not include a minimum reduction in bacterial counts (i.e., a reduction to less than 10^4 cfu/ml);
- Clinical outcomes were global assessments by the investigators and did not specifically mention the resolution of baseline signs and symptoms; and
- The primary endpoint was not a composite of both clinical and microbiological outcomes.

To the extent that these clinical trial design differences limit our use of the clinical data, our proposed clinical trial plan for tebipenem HBr with the FDA could be materially delayed and we may incur material additional costs.

Preliminary or interim data from our clinical studies that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

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

Preliminary or interim data from our clinical studies are not necessarily predictive of final data. Preliminary and interim data are subject to the risk that one or more of the clinical outcomes may materially change, as more patient data become available and we issue our final clinical study report. Preliminary or interim data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could affect our planned clinical path for tebipenem HBr, SPR720 or other product candidates we advance into clinical trials, including potentially increasing cost and/or causing delay in such development.

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

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

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

To date, patients treated with the active ingredient in tebipenem HBr have experienced drug-related side effects including diarrhea, temporary increases in hepatic enzymes, allergic reactions, rashes and convulsions. To date, tebipenem HBr has generally been well tolerated in clinical trials, and there have been no reports of serious adverse events related to tebipenem HBr, but additional adverse events may emerge in any subsequent clinical trials.

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

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

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

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

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

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

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

- the approval of other new products for the same indications;
- the timing of market introduction of the approved product as well as competitive products;
- adverse publicity about the product or favorable publicity about competitive products;
- the emergence of bacterial resistance to the product; and
- the rate at which resistance to other drugs in the target infections grows.

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

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

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

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

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

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

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

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

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

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

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

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

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

There are also a number of oral product candidates in clinical development by third parties that are intended to treat UTIs. Some mid- to late-stage product candidates include ceftibuten/clavulanate, or C-Scape, from Cipla Therapeutics, Inc., and sulopenem from Iterum Therapeutics Limited. 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, or Avycaz, from Allergan plc and Pfizer Inc., ceftolozane-tazobactam, or Zerbaxa, from Merck & Co., imipenem/cilastatin and relebactam, or Recarbrio, from Merck & Co., plazomicin, or Zemdri, from Cipla Therapeutics, Inc., cefiderocol, or Fetroja, from Shionogi & Co. Ltd., eravacycline, or Xerava, from Tetraphase Pharmaceuticals, Inc. and meropenem-vaborbactam, or Vabomere, from Melinta Therapeutics, Inc.

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

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

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

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

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

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

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

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

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

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

If we are not successful in discovering, developing and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.

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

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

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

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

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

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

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

- reduced resources for our management to pursue our business strategy;
- decreased demand for our product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant costs to defend resulting litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

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

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

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

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

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, including public health measures in place due to the ongoing COVID-19 pandemic. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

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

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

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

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

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

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

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

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

Natural disasters could severely disrupt our operations and have a material adverse effect on our business operations. If a natural disaster, health epidemic, such as COVID-19, or other event beyond our control occurred that prevented us from using all or a significant portion of our office and/or lab spaces, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult for us to continue our business for a substantial period of time.

Risks Related to Our Dependence on Third Parties

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

Although we expect to commercialize tebipenem HBr ourselves in the United States, we intend to commercialize it outside the United States through collaboration arrangements. In addition, we may seek third-party collaborators for development and commercialization of certain of our product candidates. For instance, in January 2019, we entered into a license agreement with Everest, which was amended and restated in January 2021, whereby we granted Everest an exclusive license to develop, manufacture and commercialize SPR206, or products containing SPR206, in Greater China, South Korea and certain Southeast Asian countries. Additionally, in June 2019, we entered into a collaboration agreement with the Bill and Melinda Gates Medical Research Institute, or the Gates MRI, to develop SPR720 for the treatment of lung infections caused by Mycobacterium tuberculosis. Our likely collaborators for any other marketing, distribution, development, licensing or broader collaboration arrangements we may pursue include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

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

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

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

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

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

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

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

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

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

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

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

We do not independently conduct nonclinical studies that comply with GLP requirements. We also do not have the ability to independently conduct clinical trials of any of our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials of tebipenem HBr, SPR720 or our other product candidates and expect to rely on these third parties to conduct clinical trials of our other product candidates and potential product candidates. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities and increase our costs.

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

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

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

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

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

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

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

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

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

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

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

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

For example, we have an exclusive know-how license with Meiji, or the Meiji License, that gives us rights outside of specified countries in Asia to develop, manufacture, and commercialize tebipenem HBr as well as the right to use, cross-reference, file or incorporate by reference any information and relevant Meiji regulatory documentation to support any regulatory filings outside of Asia. In addition, we have the right to develop, manufacture and have manufactured tebipenem HBr in Asia solely for the purpose of furthering development, manufacturing and commercialization of tebipenem HBr outside of Asia. In exchange for those rights, we are obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop and commercialize tebipenem HBr and to implement a specified development plan, meeting specified development milestones and providing an update on progress on an annual basis. The Meiji License requires us to pay future milestone payments of up to $2.0 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 United States 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 United States 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 United States 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 United States 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 United States government. The United States government generally takes the position that it has the right to royalty-free use of technologies that are developed under United States 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.

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

United States 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 United States 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 United States 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 United States government in procuring undelivered items from another source.

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

United States 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 United States 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 United States 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 United States government, including through our contracts with BARDA. When new technologies are developed with United States 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 United States government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to United States industry. In addition, United States government-funded inventions must be reported to the government, United States 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, changes in patent laws in the United States, including those made by 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, in the US there is an exception for one's own publication of an invention prior to filing a patent application for the invention. Most other countries have no such exception and any publication prior to filing is an absolute bar to patentability. 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 USPTO or become involved in opposition, derivation, reexamination, *inter partes* review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

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

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

We may be subject to claims that we or our employees, consultants or contractors have misappropriated the intellectual property of a third party, or claims asserting ownership of what we regard as our own intellectual property.

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

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

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

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

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

We have registered our trademarks for our name and logo in the United States and other countries and have a number of pending trademark applications in the United States and other countries. As of December 31, 2020, Spero therapeutics has two registered United States trademarks, nine registered foreign trademarks, and nine pending trademark applications. If our registered trademarks are invalidated, we may be unable to exclusively use our name or logo in certain jurisdictions or may need to change our name or logo in certain jurisdiction, which could affect our business. If we do not secure registrations for our pending trademark applications, we may encounter more difficulty in enforcing them against third parties, which could adversely affect our business. We have not yet registered trademarks for any of our product candidates in any jurisdiction. When we file trademark applications for our product candidates, those applications may not be allowed for registration, and registered trademarks may not be obtained, maintained, or enforced. During trademark registration proceedings in the United States and foreign jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but we may not be able to overcome such rejections. In addition, in the United States Patent and Trademark Office and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings.

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

Risks Related to Regulatory Approval and Other Legal Compliance Matters

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

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

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

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

We have not submitted an NDA for any of our product candidates, although we are currently preparing the NDA to seek marketing approval for tebipenem HBr for the treatment of cUTI. 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 with prior to marketing. Obtaining marketing approval for marketing of a product candidate in one country does not ensure that we will be able to obtain marketing approval in other countries, but the failure to obtain marketing approval in one jurisdiction could negatively affect our ability to obtain marketing approval in other jurisdictions. The FDA or any foreign regulatory bodies can delay, limit or deny approval of our product candidates or require us to conduct additional nonclinical or clinical testing or abandon a program for many reasons, including:

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

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

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

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

We have received fast track designation for tebipenem HBr for the treatment of complicated urinary tract infections and acute pyelonephritis, as well as fast track designation for SPR720 for treatment of adult patients with NTM-PD, and we may seek fast track designation for one or more of our other product candidates in the future. If a drug is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a drug sponsor may apply for fast track designation by the FDA for the particular indication under study. If fast track designation is obtained, the FDA may initiate review of sections of an NDA before the application is complete. This "rolling review" is available if the applicant provides and the FDA approves a schedule for the remaining information. If we seek fast track designation for a product candidate, we may not receive it from the FDA. However, even if we receive fast track designation, fast track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with fast track designation compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

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

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

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

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

If approved for commercial marketing in the United States, our lead product candidate tebipenem HBr and our other product candidates may face generic competition sooner than anticipated.

Even if we are successful in achieving regulatory approval to commercialize a product candidate, it may face competition from generic products earlier or more aggressively than anticipated, depending upon how well our future products perform in the United States prescription drug market. In addition to creating the 505(b)(2) NDA pathway, the Hatch-Waxman Amendments to the FDCA authorized the FDA to approve generic drugs that are the same as drugs previously approved for marketing under the NDA provisions of the statute pursuant to abbreviated new drug applications, or ANDAs. An ANDA relies on the preclinical and clinical testing conducted for a previously approved reference listed drug, or RLD, and must demonstrate to the FDA that the generic drug product is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug and also that it is "bioequivalent" to the RLD. The FDA is prohibited by statute from approving an ANDA when certain marketing or data exclusivity protections apply to the RLD.

If the FDA approves our future NDA for tebipenem HBr for the treatment of cUTI we expect that it will be designated by the agency as an RLD and that it will be eligible for five-year new chemical entity exclusivity under the Hatch-Waxman provisions of the FDCA. This exclusivity period would block FDA from approving either a subsequent ANDA or 505(b)(2) NDA that references our future NDA, if approved. The QIDP designation granted by FDA to this drug product and indication also make it eligible for a further five-year extension of that Hatch-Waxman exclusivity. We cannot predict the interest of potential generic competitors in the future market for such an approved treatment for cUTI, whether someone will attempt to invalidate our period of exclusivity or otherwise force the FDA to take other actions, or how quickly others may seek to come to market with competing products after the applicable exclusivity period ends. Future product candidates may also receive marketing exclusivity under the FDCA after approval that may similarly be subject to challenge or uncertainty.

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

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

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

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

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

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

- issue warning letters, untitled letters or impose holds on clinical trials if any are still on-going;
- mandate modifications to promotional materials or require provision of corrective information to healthcare practitioners;
- impose restrictions on the product or its manufacturers or manufacturing processes;

- impose restrictions on the labeling or marketing of the product;
- impose restrictions on product distribution or use;
- require post-marketing studies or clinical trials;
- require withdrawal of the product from the market;
- refuse to approve pending applications or supplements to approved applications that we submit;
- require recall of the product;
- require entry into a consent decree, which can include imposition of various fines (including restitution or disgorgement of profits or revenue), reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- suspend or withdraw marketing approvals;
- refuse to permit the import or export of the product;
- seize or detain supplies of the product; or
- issue injunctions or impose civil or criminal penalties.

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

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

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

- the federal healthcare Anti-Kickback Statute, among other things, prohibits persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federally funded healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate the statute in order to have committed a violation. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal False Claims Act imposes criminal and civil penalties, which can be enforced by private citizens through civil whistleblower and qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal ban on physician self-referrals, which prohibits, subject to certain exceptions, physician referrals of Medicare or Medicaid patients to an entity providing certain "designated health services" if the physician or an immediate family member of the physician has any financial relationship with the entity;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or for making any false statements relating to healthcare matters; as in the case of the federal healthcare Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate the statute in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, also imposes obligations on certain covered entities as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, and requires notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency or "sunshine" requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the ACA, requires manufacturers of drugs, devices, biologics and medical supplies covered by Medicare or Medicaid to report, on an annual basis, to the United States Department of Health and Human Services, or DHHS, information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, chiropractors and, beginning in 2022 for payments and other transfers of value provided in the previous year, certain advanced non-physician health care practitioners), teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; 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. For example, in November 2020, DHHS finalized significant changes to the regulations implementing the Anti-Kickback Statute, as well as the Physician Self-Referral Law (Stark Law) and the civil monetary penalty rules regarding beneficiary inducements, with the goal of offering the healthcare industry more flexibility and reducing the regulatory burden associated with those fraud and abuse laws, particularly with respect to value-based arrangements among industry participants. 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 United States 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, 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. The Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, which was signed into law on March 27, 2020 and was designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2030, in order to offset the added expense of the 2020 cancellation. The 2021 Consolidated Appropriations Act was subsequently signed into law on December 27, 2020 and extends the CARES Act suspension period to March 31, 2021.

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. There have been several United States 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. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers, or PBMs, and other members of the health care and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area.

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 United States 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.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. We expect that additional state and federal health care reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for health care products and services. Moreover, the Biden Administration, including his nominee for Secretary of DHHS, has indicated that lowering prescription drug prices is a priority, but we do not yet know what steps the administration will take or whether such steps will be successful.

If we successfully commercialize one of our product candidates, failure to comply with our reporting and payment obligations under United States 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 United States 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.

Additionally, the 2021 Consolidated Appropriations Act signed into law on December 27, 2020 incorporated extensive healthcare provisions and amendments to existing laws, which includes a requirement that all manufacturers of drug products covered under Medicare Part B report the product's average sales price, or ASP, to DHHS beginning on January 1, 2022, subject to enforcement via civil money penalties.

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.

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

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

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the United States 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.

Separately, in response to the COVID-19 pandemic and public health emergency declaration in the United States, on March 10, 2020, the FDA announced its intention to temporarily postpone most inspections of foreign manufacturing facilities and products. On March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials, which has been updated periodically since that time with common questions and answers. As of January 29, 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals and conducting mission-critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. As of October 2020, Utilizing a rating system to assist in determining when and where it is safest to conduct such inspections based on data about the virus's trajectory in a given state and locality and the rules and guidelines that are put in place by state and local governments, FDA is either continuing to, on a case-by-case basis, conduct only mission-critical inspections, or, where possible to do so safely, resuming prioritized domestic inspections, which generally include pre-approval inspections. Foreign pre-approval inspections that are not deemed mission-critical remain postponed, while those deemed mission-critical will be considered for inspection on a case-by-case basis. FDA will use similar data to inform resumption of prioritized operations abroad as it becomes feasible and advisable to do so, and it has recently resumed inspections in China and plans to also resume such activities in India as soon as possible. The FDA may not be able to maintain this pace and delays or setbacks are possible in the future.

Should FDA determine that an inspection is necessary for NDA approval and an inspection cannot be completed during the review cycle due to restrictions on travel, FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, FDA may defer action on the application until an inspection can be completed. Additionally, regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown recurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, 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.

If a prolonged government shutdown or slowdown occurs, it could significantly affect the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Risks Related to Employee Matters and Managing Growth

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Our Common Stock

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

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

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

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

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

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

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

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

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

We have in the past issued, and we may at any time in the future issue, shares of preferred stock. In connection with our July 2018 public offering, we issued 2,220 shares of our Series A Convertible Preferred Stock, or Series A Preferred Stock, to certain affiliates of Biotechnology Value Fund, L.P., or BVF, each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. In November 2018, we entered into an exchange agreement with BVF to exchange 1,000,000 shares of our common stock previously held by BVF for 1,000 shares of our Series B Convertible Preferred Stock, or Series B Preferred Stock, each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. In June 2019, BVF converted 500 shares of Series A Preferred Stock into 500,000 shares of our common stock pursuant to BVF's rights under the certificate of designation for such Series A Preferred Stock. In December 2020, BVF converted the remaining 1,720 shares of Series A Preferred Stock into 1,720,000 shares of our common stock pursuant to BVF's rights under the certificate of designation for such Series A Preferred Stock. In connection with our rights offering, which we launched in February 2020 and closed in early March 2020, we issued 2,287 shares of our Series C Preferred Stock to BVF. In September 2020, in connection with our underwritten public offering, we issued 3,215,000 shares of our Series D Preferred Stock to BVF. If BVF or any other future holders of our shares of preferred stock convert their shares into common stock, existing holders of our common stock will experience dilution.

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

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

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years. We would cease to be an emerging growth company upon the earlier of: (i) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of our initial public offering, which is December 31, 2022; (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC which means the first day of the year following the first year in which the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of June 30th. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or Sarbanes-Oxley, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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

We are subject to Section 404 of The Sarbanes-Oxley Act of 2002, or Section 404, and the related rules of the SEC, which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Beginning with our next annual report that we will be required to file with the SEC, Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting. However, for so long as we remain an emerging growth company as defined in the JOBS Act, or a "smaller reporting company" (SRC) and non-accelerated filer, we intend to take advantage of certain exemptions from various reporting requirements, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404. Once we are no longer an emerging growth company and otherwise do not meet the definition of a SRC and non-accelerated filer or, if prior to such date, we opt to no longer take advantage of the applicable exemption, we will be required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal controls over financial reporting. We could qualify as a SRC if the market value of our common stock held by non-affiliates is below $250 million (or $700 million if our annual revenue is less than $100 million) as of June 30 in any given year.

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

As a public company, and particularly after we are no longer an “emerging growth company,” we incur significant legal, accounting and other expenses that we did not incur as a private company. Sarbanes-Oxley, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly. For example, these rules and regulations have made it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

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

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

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

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

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

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

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

As of December 31, 2020, 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 45% 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, or the DGCL, 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.

In addition, our amended and restated certificate of incorporation, to the fullest extent permitted by law, provides that the Court of Chancery of the State of Delaware will be the exclusive forum for: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our amended and restated certificate of incorporation, or our amended and restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. This exclusive forum provision does not apply to suits brought to enforce a duty or liability created by the Exchange Act. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision and asserts claims under the Securities Act, inasmuch as Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rule and regulations thereunder. There is uncertainty as to whether a court would enforce such provision with respect to claims under the Securities Act, and our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, results of operations and financial condition.

Provisions in our charter and other provisions of Delaware law could limit the price that investors are willing to pay in the future for shares of our common stock.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

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

Item 3. Legal Proceedings.

We are not party to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

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

Holders of Record

As of March 8, 2021, we had approximately nine stockholders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

Dividends

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

Purchases of Equity Securities by the Issuer

None.

Item 6. Selected Financial Data.

Not applicable.

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

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

Overview

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

We have experienced net losses and significant cash outflows from cash used in operating activities since our inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. As of December 31, 2020, we had an accumulated deficit of $277.7 million, and cash, cash equivalents and marketable securities of $126.9 million. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. Based on our current plans, we believe that our existing cash, cash equivalents and marketable securities, together with the committed funding from our existing BARDA contract and other non-dilutive funding commitments, will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2022, including through the submission of the NDA for tebipenem HBr. This timeline is subject to uncertainty as to the timing of future expenditures. We have developed plans to mitigate this risk, which primarily consist of raising additional capital through some combination of equity or debt financings, potential new collaborations, additional grant funding and/or reducing cash expenditures. If we are not able to secure adequate additional funding, we plan to make reductions in spending. In that event, we may have to delay, scale back, or eliminate some or all of our planned clinical trials and research stage programs. The actions necessary to reduce spending under this plan at a level that mitigates the factors described above is not considered probable, as defined in the accounting standards and therefore, the full extent to which management may extend our funds through these actions may not be considered in management's assessment of our ability to continue as a going concern. As a result, management has concluded that substantial doubt exists about our ability to continue as a going concern.

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

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

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

Recent Developments

Business Update regarding COVID-19

The spread of SARS-CoV-2, and the resulting disease COVID-19 in 2020, has caused an economic downturn on a global scale, as well as widespread business disruptions and significant volatility in the financial markets. In March 2020, the World Health Organization declared COVID-19 a pandemic. In response to the pandemic, we implemented and have maintained a remote working policy for all employees to aid the global containment effort.

Update on Phase 2a Clinical Trial

On February 5, 2021, we announced that the FDA informed us that a clinical hold had been placed on our Phase 2a clinical trial of SPR720, following our notification to the FDA of our decision to pause dosing in our ongoing Phase 2a clinical trial of SPR720 as a precautionary measure related to events in our ongoing animal toxicology study of SPR720. The decision to implement the pause was made based on a recommendation from the Company's Safety Review Board, or SRB, following review of data from an ongoing toxicology study of SPR720 in adult non-human primates in which mortalities with inconclusive causality to treatment were observed.

The animal study is being conducted to assess the potential toxicity of SPR720. A concurrent study of SPR720 in rats is proceeding uneventfully. These studies are meant to support longer-term treatment with SPR720 beyond the 28 days currently supported by IND-enabling toxicology studies. No serious adverse events have been observed in any human study participants.

Subsequent to receiving verbal notification from the FDA of the clinical hold, we received a formal clinical hold letter in which the FDA has requested additional information from the non-human primate trial, including a study report. We have decided to discontinue the Phase 2a clinical trial at this time to best facilitate future potential adjustments to the protocol based on FDA feedback and to avoid incurring costs associated with the trial while on clinical hold. We are continuing to work with the FDA to evaluate the findings and determine the further development pathway for the SPR720 clinical program.

Components of Our Results of Operations

Grant Revenue

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

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

Collaboration Revenue

Collaboration revenue relates to our agreement with Everest.

Operating Expenses

Research and Development Expenses

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

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

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.

In June 2019, we entered into a collaboration with Gates MRI, a nonprofit research institution wholly owned by the Bill and Melinda Gates Foundation to develop SPR720 for the treatment of lung infections caused by Mtb. In furtherance of the Gates MRI's charitable purposes, we also granted the Gates MRI a no cost, exclusive license to develop, manufacture and commercialize SPR720 for the treatment of TB in low- and middle- income countries. Gates MRI will conduct and fund preclinical and clinical studies for the development of SPR720 against TB and fund certain agreed upon collaborative research activities performed by us. Due to our assessment that we do not have a vendor/customer relationship with the Gates MRI, we recognize the funding received under the agreement as a reduction to the research and development expenses as the related expenses are incurred.

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

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

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

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, including on account of the disruptive impacts of the COVID-19 pandemic;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers to obtain manufacturing supply;

- obtainment and maintenance of patent, trade secret protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain our license agreement with Meiji with respect to tebipenem HBr;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales of tebipenem HBr and our other product candidates, if approved, whether alone or in collaboration with others;
- acceptance of tebipenem HBr and our other product candidates, if approved, by patients, the medical community and third-party payors;
- competition with other therapies; and
- a continued acceptable safety profile of tebipenem HBr and our other product candidates, if approved.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs and timing associated with the development of that product candidate. We may never succeed in obtaining regulatory approval for any of our product candidates.

General and Administrative Expenses

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

Other Income (Expense)

Anti-Dilution Rights. In connection with the issuance of non-controlling interests in certain of our subsidiaries, specifically Spero Gyrase, Inc., we granted the minority investors the right to maintain ownership interests at no additional cost, subject to a maximum ownership percentage, which rights we refer to collectively as anti-dilution rights. We classified the anti-dilution rights as derivative liabilities on our consolidated balance sheet that we remeasured to fair value at each reporting date, and we recognized changes in the fair value of the derivative liabilities associated with the anti-dilution rights as a component of other income (expense) in our consolidated statement of operations and comprehensive loss. In November 2019, we repurchased 100% of the minority investor's outstanding shares in Spero Gyrase, Inc. at a price of $0.001 per share. As a result, as of December 31, 2020 and 2019, there are no anti-dilution rights outstanding. Additionally, effective as of January 1, 2020, we merged Spero Gyrase, Inc. with and into Spero, Therapeutics, Inc.

Interest Income

Interest income consists of interest earned on our cash equivalents, which are primarily invested in money market accounts, as well as interest earned on our investments in marketable securities that we held during the years ended December 31, 2020 and 2019.

Other Income (Expense), Net

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, 2020, we had federal and state net operating loss carryforwards of $228.1 million and $226.2 million, respectively, which may be available to offset future income tax liabilities. The federal NOLs of $73.0 million will expire at various dates from 2033 to 2037 and approximately $155.1 million can be carried forward indefinitely. The state NOLs begin to expire in 2033 and will expire at various dates through 2039. In addition, as of December 31, 2020, we had foreign net operating loss carryforwards of $10.7 million, which may be available to offset future income tax liabilities and do not expire. As of December 31, 2020, we also had federal and state research and development tax credit carryforwards of $6.7 million and $1.4 million, respectively, which begin to expire in 2033 and 2028, respectively. We have recorded a full valuation allowance against our net deferred tax assets at each balance sheet date.

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 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. Revenue from government grants is recognized as the qualifying expenses related to the contracts are incurred, provided that there is reasonable assurance of recoverability. Revenue recognized upon incurring qualifying expenses in advance of receipt of funding is recorded as unbilled receivables, a component of prepaid expenses and other current assets, in the consolidated balance sheet.

We recognize funding received from BARDA, the DoD and the NIAID of the NIH, as revenue, rather than as a reduction of research and development expenses, because we are the principal in conducting the research and development activities and these contracts are central to our ongoing operations. We recognize revenue only after the qualifying expenses related to the contracts have been incurred, we are reasonably assured that the expenses will be reimbursed and the revenue is collectible. We record revenue recognized upon incurring qualifying expenses in advance of billing as unbilled revenue, which is included in other receivables in our consolidated balance sheet. The related costs incurred by us are included in research and development expense in our consolidated statements of operations and comprehensive loss.

Collaboration Agreements

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

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

Accrued Research and Development Expenses

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

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

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

Share-Based Compensation

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

Results of Operations

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

Comparison of the Years Ended December 31, 2020 and 2019

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

	Year Ended December 31, 2020	2019	$ Change
Revenues:			
Grant revenue	$ 9,072	$ 13,405	$ (4,333)
Collaboration revenue	258	4,742	(4,484)
Total revenues	9,330	18,147	(8,817)
Operating expenses:			
Research and development	67,003	65,775	1,228
General and administrative	21,440	15,588	5,852
Total operating expenses	88,443	81,363	7,080
Loss from operations	(79,113)	(63,216)	(15,897)
Other income (expense):			
Gain on settlement of derivative liability	-	223	(223)
Interest income	401	1,328	(927)
Other income (expense), net	432	740	(308)
Total other income (expense), net	833	2,291	(1,458)
Net loss	$ (78,280)	$ (60,925)	$ (17,355)

Grant Revenue

	Year Ended December 31, 2020	2019	$ Change
BARDA Contract (Tebipenem HBr)	$ 7,929	$ 12,082	$ (4,153)
NIAID Contract (SPR206)	719	1,021	(302)
NIAID Award (SPR720)	40	77	(37)
DoD Agreement (Potentiator product candidates)	384	225	159
Total revenue	$ 9,072	$ 13,405	$ (4,333)

Grant revenue recognized during 2020 and 2019 consisted of the reimbursement of qualifying expenses incurred in connection with our various government awards. The decrease in revenue during 2020 was primarily due to decreased funding received under our BARDA contract for tebipenem HBr.

Collaboration Revenue

During the years December 31, 2020 and 2019, we recognized $0.3 million and $4.7 million of revenue, respectively, related to our agreement with Everest, consisting of the performance of research and development services.

Research and Development Expenses

	Year Ended December 31, 2020	2019	$ Change
Direct research and development expenses by program:			
Tebipenem HBr	$ 41,923	$ 43,440	$ (1,517)
SPR720	3,816	3,741	75
Potentiator product candidates (SPR206 and SPR741)	1,626	3,617	(1,991)
Unallocated expenses:			
Personnel related (including share-based compensation)	15,014	10,967	4,047
Facility related and other	4,624	4,010	614
Total research and development expenses	$ 67,003	$ 65,775	$ 1,228

Direct costs related to our tebipenem HBr program decreased by $1.5 million during 2020 compared to 2019 primarily due to the completion of significant activities and related costs of the Phase 3 clinical trial in 2020. We initiated enrollment for the phase 3 clinical trial in the first quarter of 2019, completed enrollment in the second quarter of 2020 and announced results of topline data in September 2020. This decrease was partially offset by increases in expenses related to formulation development, manufacturing process and manufacturing of clinical trial material in 2020 compared to 2019. We expect to continue to incur direct costs related to tebipenem HBr as we finalize activities in the Phase 3 clinical trial and incur expenses related to a potential NDA filing for tebipenem HBr.

Direct costs related to our SPR720 program increased by $0.1 million during 2020 compared to 2019, primarily due to increased expenses related to the initiation of our Phase 2a clinical trial, offset by decreased costs related to the formulation development, manufacturing process and manufacturing of clinical trial material. Direct costs related to our SPR720 program during the year ended December 31, 2020 reflect a $2.1 million reduction to expense related to activities funded by Gates MRI, compared to $1.7 million during the year ended December 31, 2019. On February 5, 2021, we announced that the FDA informed us that a clinical hold had been placed on our Phase 2a clinical trial of SPR720, which is further described elsewhere in this "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of our Annual Report on Form 10-K under the heading "Recent Developments – Update on Phase 2a Clinical Trial."

Direct costs related to our Potentiator product candidates include costs related to our SPR206 and SPR741 programs. Direct costs related to our SPR206 program decreased by $2.0 million during 2020, primarily due to higher costs incurred in the prior year related to the Phase 1 trial. Direct costs related to our SPR741 program were immaterial for both the years ended December 31, 2020 and 2019. In January 2020, we decided to proceed with SPR206 as the lead Potentiator product candidate and discontinue development of SPR741.

During 2020 and 2019, research and development expenses conducted by our Australian subsidiary were recorded net of a 43.5% research and development tax incentive for qualified expenses from the Australian government, resulting in a receivable of $1.2 million.

The increase in personnel-related costs included in unallocated expenses of $4.0 million was primarily due to an increase in research and development headcount and a $0.6 million increase in share-based compensation.

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

General and Administrative Expenses

	Year Ended December 31,		
	2020	2019	$ Change
Personnel related (including share-based compensation)	$ 10,661	$ 8,050	$ 2,611
Professional and consultant fees	8,271	5,849	2,422
Facility related and other	2,508	1,689	819
Total general and administrative expenses	$ 21,440	$ 15,588	$ 5,852

The increase in personnel-related costs of $2.6 million was primarily a result of an increase in headcount in our general and administrative function. Personnel-related costs for the years ended December 31, 2020 and 2019 included share-based compensation expense of $2.7 million and $2.2 million, respectively.

The increase in professional and consultant fees of $2.4 million primarily related to increased commercial operations expenses, as well as increased IT, HR and Finance contractor and consulting expenses related to supporting the growth in our business.

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 $0.8 million during 2020, compared to $2.3 million during 2019. Other income, net in the year ended December 31, 2020 was primarily comprised of unrealized foreign currency gains, offsetting decreased interest income due to falling interest rates. In comparison, other income, net, for the year ended December 31, 2019 consisted of other income of $2.1 million, which was primarily related to interest income on our invested cash balances and marketable securities, as well as $0.2 million in connection with the repurchase of Vaxart Inc.'s outstanding shares in Spero Gyrase, Inc. at a price of $0.001 per share.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We have recognized limited revenue to date from funding arrangements with the DoD, NIAID, CARB-X and BARDA and our license agreement with Everest. We have not yet commercialized any of our product candidates and we do not expect to generate revenue from sales of any product candidates for several years, if at all. To date, we have funded our operations with proceeds from the sales of preferred units and bridge units, payments received under license and collaboration agreements and funding from government contracts, and from multiple equity financings of our common and preferred stock. As of December 31, 2020, we had cash, cash equivalents and marketable securities of $126.9 million.

On September 15, 2020, we completed an underwritten public offering of an aggregate of 4,785,000 shares of our common stock and 3,215,000 shares of our Series D Preferred Stock. The price to the public in the offering was $10.00 per share with respect to the common stock and the Series D Preferred Stock. In addition, under the terms of the Underwriting Agreement, we granted the underwriters an option, exercisable for 30 days, to purchase up to 1,200,000 additional shares of common stock.

The shares of Series D Preferred Stock are convertible on a one-to-one basis into shares of common stock at any time at the option of the holder, provided that the holder will be prohibited from converting the Series D 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 D Preferred Stock will receive a payment equal to $0.001 per share of Series D Preferred Stock before any proceeds are distributed to the holders of common stock and equal to any distributions to the holders of Series A Preferred Stock, Series B Preferred Stock and Series C Preferred Stock. Shares of Series D Preferred Stock will generally have no voting rights, except as required by law and except that the consent of holders of a majority of the then outstanding Series D Preferred Stock will be required to amend the terms of the Series D Preferred Stock. As such, we have classified the Series D Convertible Preferred Stock within permanent equity in its consolidated balance sheet.

The offering closed on September 15, 2020 with an aggregate public offering price of $80.0 million. Aggregate net proceeds from the offering were $74.7 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

In addition, pursuant to the Underwriting Agreement, on October 1, 2020, we issued and sold 1,200,000 shares of common stock at the price of $10.00 per share pursuant to the underwriters' exercise of their option to purchase additional shares of common stock, resulting in additional net proceeds of approximately $11.2 million after deducting underwriting discounts and commissions.

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

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

At the closing of the rights offering on March 5, 2020, a total of 1,046,249 shares of our common stock and 2,287 shares of Series C Preferred Stock were issued for aggregate gross proceeds of $30.0 million. Issuance costs related to the offering were $0.5 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, 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," or ATM, offering as defined in Rule 415 of the Securities Act, subject to the terms of the sales agreement.

The prospectus underlying the "at-the-market" offering program was terminated on September 9, 2020 in connection with our underwritten public offering that was completed in September 2020. At such time, we had raised approximately $15.4 million in sales of our common stock under the "at-the-market" offering program, prior to deducting sales commissions, and had remaining available capacity of approximately $34.6 million. On November 13, 2020, we reinstated the "at-the-market" offering program with a capacity of up to $34 million by filing an updated prospectus.

During the year ended December 31, 2020, we sold 993,870 shares of our common stock under the "at-the-market" agreement at an average price of approximately $13.66 per share for aggregate gross proceeds of approximately $13.6 million prior to deducting sales commissions.

Concurrently with the filing of this Annual Report on Form 10-K, we entered into a new sales agreement with Cantor and will file a new universal shelf registration statement on Form S-3, including an "at-the-market" prospectus with the SEC, which is further described elsewhere in this Annual Report on Form 10-K under "Item 9B. Other Events." Our existing sales agreement with Cantor will terminate automatically at such time as the SEC declares effective our new universal shelf registration statement on Form S-3.

The COVID-19 pandemic has resulted in ongoing volatility in financial markets. If our access to capital is restricted or associated borrowing costs increase as a result of developments in financial markets relating to the COVID-19 pandemic, our operations and financial condition could be adversely impacted.

Cash Flows

The following table summarizes our sources and uses of cash for the years ended December 31, 2020 and 2019:

	Year Ended December 31,	
	2020	2019
Cash used in operating activities	$ (85,872)	$ (50,020)
Cash provided by (used in) investing activities	10,470	29,530
Cash provided by financing activities	130,881	16,140
Net increase (decrease) in cash and cash equivalents	$ 55,479	$ (4,350)

Operating Activities

Net cash used in operating activities for the year ended December 31, 2020 was $85.9 million, primarily resulting from our net loss of $78.3 million, adjusted for net non-cash items of $5.9 million (primarily stock-based compensation and depreciation and amortization expense). Net cash used in changes in our operating assets and liabilities was $(13.5) million and consisted primarily of a decrease of $12.1 million in accrued expenses and accounts payable, a $1.9 million increase in other assets and a $1.2 million increase in prepaid expenses and other current assets, partially offset by a $2.2 million net decrease in receivables related to our government awards.

Net cash used in operating activities for the year ended December 31, 2019 was $50.0 million, primarily resulting from our net loss of $60.9 million, adjusted for net non-cash items of $4.1 million (primarily stock-based compensation and depreciation and amortization expense). Net cash provided by changes in our operating assets and liabilities was $6.8 million and consisted primarily of an increase of $13.8 million in accrued expenses and accounts payable and a $2.7 million decrease in prepaid expenses and other current assets, offset by a $7.1 million increase in receivables related to our government awards and a $2.9 million increase in other assets.

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

Investing Activities

Net cash provided by investing activities for the year ended December 31, 2020 was $10.5 million, primarily related to the maturities of marketable securities of $56.4 million, offset by purchases of marketable securities of $45.7 million.

Net cash provided by investing activities for the year ended December 31, 2019 was $29.5 million and consisted primarily of the net maturities of marketable securities, as well as $0.3 million in property and equipment purchases.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2020 was $130.9 million, consisting primarily of proceeds of $116.5 million from the sale of common stock, Series C Preferred Stock and Series D Preferred Stock in our rights offering and underwritten public offering, net proceeds of $13.2 million from the sale of common stock under our "at-the-market" offering program sales agreement and proceeds of $2.2 million from the exercise of employee stock options, offset by the payment of offering expenses of approximately $1.0 million.

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

Funding Requirements

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

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

As of December 31, 2020, we had cash, cash equivalents and marketable securities of $126.9 million. In accordance with Accounting Standards Update, or ASU, 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40), we are required to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern from the issuance date of our financial statements. Based on our current plans, we believe that our existing cash, cash equivalents and marketable securities, together with the committed funding from our existing BARDA contract and other non-dilutive funding commitments, will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2022, including through the submission of the NDA for tebipenem HBr.

This timeline is subject to uncertainty as to the timing of future expenditures. We have developed plans to mitigate this risk, which primarily consist of raising additional capital through some combination of equity or debt financings, potential new collaborations, additional grant funding and/or reducing cash expenditures. If we are not able to secure adequate additional funding, we plan to make reductions in spending. In that event, we may have to delay, scale back, or eliminate some or all of our planned clinical trials, research stage programs and commercial activities. The actions necessary to reduce spending under this plan at a level that mitigates the factors described above is not considered probable, as defined in the accounting standards and therefore, the full extent to which management may extend our funds through these actions may not be considered in management's assessment of our ability to continue as a going concern. As a result, management has concluded that substantial doubt exists about our ability to continue as a going concern.

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. The COVID-19 pandemic has resulted in ongoing volatility in financial markets. If our access to capital is restricted or associated borrowing costs increase as a result of developments in financial markets, including relating to the COVID-19 pandemic, our operations and financial condition could be adversely impacted. 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, 2020 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)	10,876	947	3,352	3,464	3,113
Total	$ 10,876	$ 947	$ 3,352	$ 3,464	$ 3,113

(1) Reflects payments due for our lease of office space under an operating lease agreement that expires in 2027.

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 future milestone payments of up to $2.0 million upon the achievement of specified clinical and regulatory milestones for tebipenem HBr, (ii) to pay royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement and (iii) to pay to Meiji a low double-digit percentage of any sublicense fees received by us up to $7.5 million. During the fourth quarter of 2018 we paid Meiji approximately $1.6 million related to fixed assets which will be used in manufacturing related activities at Meiji. The equipment has been capitalized as property and equipment in the consolidated balance sheet as of December 31, 2020 and 2019.

Under an agreement we entered into with PBB, we are obligated to make milestone payments of up to $5.8 million upon the achievement of specified clinical milestones and a payment of £5.0 million ($6.8 million as of December 31, 2020) upon the achievement of a specified commercial milestone for SPR206. In addition, we have agreed to pay to PBB royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement.

Under our agreement with Vertex, we are obligated to make future milestone payments of up to $80.2 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 year ended December 31, 2020, we paid Vertex $0.9 million related to the achievement of regulatory milestones for SPR720.

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

Off-Balance Sheet Arrangements

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

Recently Adopted Accounting Pronouncements

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

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

As of December 31, 2020, we had cash, cash equivalents and marketable securities of $126.9 million, consisting of cash, money market accounts, corporate bonds, commercial paper and United States 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 United States interest rates. If market interest rates were to increase immediately and uniformly by 50 basis points, from levels as of December 31, 2020, the net fair value of our interest sensitive marketable securities would hypothetically decline by $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 United States 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, 2020 and 2019, and the related consolidated statements of operations and comprehensive loss, of convertible preferred shares and stockholders' equity and of cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

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

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

Basis for Opinion

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

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

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

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 11, 2021

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, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 85,209	$ 29,730
Marketable securities	41,697	52,315
Other receivables	5,330	7,760
Tax incentive receivable, current	846	786
Prepaid expenses and other current assets	6,063	4,823
Total current assets	139,145	95,414
Property and equipment, net	1,669	2,273
Tax incentive receivable	311	21
Operating lease right-of-use assets	7,114	4,875
Other assets	5,212	3,520
Total assets	$ 153,451	$ 106,103
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,155	$ 4,147
Accrued expenses and other current liabilities	12,241	21,588
Operating lease liabilities	947	928
Total current liabilities	14,343	26,663
Non-current operating lease liabilities	6,891	4,617
Other long-term liabilities	177	249
Total liabilities	21,411	31,529
Commitments and contingencies (Note 12)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized, 3,218,287 shares issued and outstanding as of December 31, 2020 and 2,720 shares issued and outstanding as of December 31, 2019	3	—
Common stock, $0.001 par value; 60,000,000 shares authorized as of December 31, 2020 and December 31, 2019; 29,260,247 shares issued and outstanding as of December 31, 2020 and 19,190,695 shares issued and outstanding as of December 31, 2019	29	19
Additional paid-in capital	409,722	273,966
Accumulated deficit	(277,707)	(199,427)
Accumulated other comprehensive gain (loss)	(7)	16
Total stockholders' equity	132,040	74,574
Total liabilities and stockholders' equity	$ 153,451	$ 106,103

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,	
	2020	2019
Revenues:		
Grant revenue	$ 9,072	$ 13,405
Collaboration revenue	258	4,742
Total revenues	9,330	18,147
Operating expenses:		
Research and development	67,003	65,775
General and administrative	21,440	15,588
Total operating expenses	88,443	81,363
Loss from operations	(79,113)	(63,216)
Other income (expense):		
Gain on settlement of derivative liability	—	223
Interest income	401	1,328
Other income (expense), net	432	740
Total other income (expense), net	833	2,291
Net loss	$ (78,280)	$ (60,925)
Net loss per share attributable to common stockholders, basic and diluted	$ (3.52)	$ (3.35)
Weighted average common shares outstanding, basic and diluted:	22,386,122	18,160,525
Comprehensive loss:		
Net loss	(78,280)	(60,925)
Other comprehensive gain (loss):		
Unrealized gain (loss) on marketable securities	(23)	38
Reclassification adjustment for gains included in net loss	—	6
Net unrealized gains (losses) on securities	(23)	44
Total comprehensive loss	$ (78,303)	$ (60,881)

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

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

	Series A, B, C and D Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Accumulated Other Comprehensive	Spero Therapeutics, Inc. Stockholders'	Non-controlling	Total Stockholders'
	Shares	Par Value	Shares	Par Value	Capital	Deficit	Income (Loss)	Equity (Deficit)	Interests	Equity (Deficit)
Balances at December 31, 2018	**3,220**	**—**	**17,205,962**	**17**	**254,013**	**(138,502)**	**(28)**	**115,500**	**355**	**115,855**
Issuance of common stock upon the exercise of stock options	—	—	78,610	—	508	—	—	508	—	508
Issuance of common stock, net of issuance costs of $474	—	—	1,406,123	1	15,315	—	—	15,316	—	15,316
Conversion of convertible preferred stock to common stock	(500)	—	500,000	1	(1)	—	—	—	—	—
Share-based compensation expense	—	—	—	—	3,776	—	—	3,776	—	3,776
Purchase of non-controlling interest in Spero Gyrase, Inc.	—	—	—	—	355	—	—	355	(355)	—
Unrealized gain on available-for-sale securities	—	—	—	—	—	—	44	44	—	44
Net loss	—	—	—	—	—	(60,925)	—	(60,925)	—	(60,925)
Balances at December 31, 2019	**2,720**	**—**	**19,190,695**	**19**	**273,966**	**(199,427)**	**16**	**74,574**	**—**	**74,574**
Issuance of common stock upon the exercise of stock options	—	—	324,433	—	2,189	—	—	2,189	—	2,189
Issuance of common stock, net of offering costs of $731 and net of issuance costs	—	—	8,025,119	8	77,921	—	—	77,929	—	77,929
Issuance of Series C preferred stock, net of offering costs of $41	2,287	—	—	—	20,542	—	—	20,542	—	20,542
Beneficial conversion feature of Series C preferred stock	—	(549)	—	—	549	—	—	—	—	—
Deemed dividends related to immediate accretion of beneficial conversion feature of Series C preferred stock	—	549	—	—	(549)	—	—	—	—	—
Issuance of Series D preferred stock, net of offering costs of $181	3,215,000	3	—	—	30,218	—	—	30,221	—	30,221
Conversion of convertible preferred stock to common stock	(1,720)	—	1,720,000	2	(2)	—	—	—	—	—
Share-based compensation expense	—	—	—	—	4,888	—	—	4,888	—	4,888
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	(23)	(23)	—	(23)
Net loss	—	—	—	—	—	(78,280)	—	(78,280)	—	(78,280)
Balances at December 31, 2020	**3,218,287**	**3**	**29,260,247**	**29**	**409,722**	**(277,707)**	**(7)**	**132,040**	**—**	**132,040**

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

SPERO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,	
	2020	2019
Cash flows from operating activities:		
Net loss	$ (78,280)	$ (60,925)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	761	750
Non-cash lease cost	585	408
Loss on disposal of fixed assets	—	184
Gain on settlement of derivative liability	—	(223)
Share-based compensation	4,888	3,776
Realized (gain) loss on investments	—	(1)
Unrealized foreign currency transaction (gain) loss	(330)	(18)
Accretion of discount on marketable securities	(32)	(750)
Changes in operating assets and liabilities:		
Other receivables	2,430	(7,384)
Prepaid expenses and other current assets	(1,240)	2,654
Tax incentive receivables	(254)	299
Other assets	(1,890)	(2,912)
Accounts payable	(2,975)	564
Accrued expenses and other current liabilities	(9,130)	13,272
Other long-term liabilities	(72)	(52)
Operating lease liabilities	(333)	338
Net cash used in operating activities	(85,872)	(50,020)
Cash flows from investing activities:		
Purchases of marketable securities	(45,723)	(88,993)
Proceeds from maturities of marketable securities	56,350	118,837
Purchases of property and equipment	(157)	(314)
Net cash provided by investing activities	10,470	29,530
Cash flows from financing activities:		
Proceeds from the issuance of common stock, net of commissions	13,166	15,790
Proceeds from the issuance of common stock related to Rights Offering	9,416	—
Proceeds from the issuance of common stock related to the Underwritten Public Offering	56,078	—
Proceeds from issuance of Series C Preferred Shares related to Rights Offering	20,583	—
Proceeds from issuance of Series D Preferred Shares related to the Underwritten Public Offering	30,402	—
Payment of offering costs	(953)	(158)
Proceeds from stock option exercises	2,189	508
Net cash provided by financing activities	130,881	16,140
Net increase (decrease) in cash and cash equivalents	55,479	(4,350)
Cash and cash equivalents at beginning of period	29,730	34,080
Cash and cash equivalents at end of period	$ 85,209	$ 29,730
Supplemental disclosure of non-cash activities:		
Right-of-use assets and lease obligations recorded upon commencement or amendment of lease agreements	$ 2,626	$ 1,038

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

1. Nature of the Business and Basis of Presentation

Spero Therapeutics, Inc., together with its consolidated subsidiaries (the "Company" or "Spero"), is a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing and commercializing treatments in high unmet need areas involving multi-drug resistant, or MDR, bacterial infections and rare diseases. The Company's most advanced product candidate, tebipenem pivoxil hydrobromide or tebipenem HBr (previously SPR994), is designed to be the first oral carbapenem-class antibiotic for use in adults to treat MDR Gram-negative infections. Treatment with effective orally administrable antibiotics may prevent hospitalizations for serious infections and enable earlier, more convenient and cost-effective treatment of patients after hospitalization. The Company is also developing SPR720, a novel oral antibiotic designed for the treatment of a rare, orphan disease caused by pulmonary non-tuberculous mycobacterial infections, or NTM disease. In addition, the Company has a Potentiator technology, that includes an IV-administered product candidate, SPR206, being developed to treat MDR Gram-negative infections in the hospital.

The Company was formed as Spero Therapeutics, LLC in December 2013 under the laws of the State of Delaware. On June 30, 2017, through a series of transactions, Spero Therapeutics, LLC merged with and into Spero Therapeutics, Inc. (formerly known as Spero OpCo, Inc.), a Delaware corporation.

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 prospectus underlying the "at-the-market" offering program was terminated on September 9, 2020 in connection with the Company's underwritten public offering that was completed in September 2020. At such time, the Company had raised approximately $15.4 million in sales of its common stock under the "at-the-market" offering program, prior to deducting sales commissions, On November 13, 2020, the Company reinstated the "at-the-market" offering program for the remaining available capacity of $34.0 million by filing an updated prospectus.

Concurrently with the filing of this Annual Report on Form 10-K, the Company entered into a new sales agreement with Cantor and will be filing a new universal shelf registration statement on Form S-3, including an "at-the-market" prospectus with the SEC, which is further described elsewhere in this Annual Report on Form 10-K under "Item 9B. Other Events." The Company's existing sales agreement with Cantor will terminate automatically at such time as the SEC declares effective the Company's new universal shelf registration statement on Form S-3.

The Company is subject to risks and uncertainties common to 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, risks of failure or unsatisfactory results of nonclinical studies and clinical trials, the need to obtain marketing approval for its product candidates, the need to successfully commercialize and gain market acceptance of its product candidates and the ability to secure additional capital to fund operations. The Company's product candidates will require additional 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. The pandemic caused by COVID-19 has resulted, and is likely to continue to result, in significant national and global economic disruption and may adversely affect our business. The Company has experienced impacts to its clinical and development timelines due to the worldwide spread of COVID-19. However, to date, the Company has not experienced material impacts to liquidity, nor has it incurred impairment of any assets as a result of COVID-19. The Company continues to monitor this situation and the possible effects on its business, results of operations and financial condition, including manufacturing, clinical trials, research and development costs and employee-related amounts.

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.

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, funding from government contracts, a licensing agreement and through the sale of the Company's common and preferred stock. The Company has incurred recurring losses since inception, including net losses of $78.3 million and $60.9 million for the years ended December 31, 2020 and 2019, respectively. In addition, as of December 31, 2020, the Company had an accumulated deficit of $277.7 million. The Company expects to continue to generate operating losses for the foreseeable future.

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 these consolidated financial statements are issued. Based on the Company's current operating plan and existing cash, cash equivalents and marketable securities, the Company has determined that there is substantial doubt regarding its ability to continue as a going concern. The Company will require additional funding to fund the development of its product candidates through regulatory approval and commercialization, and to support its continued operations. The Company will seek additional funding through public or private financings, debt financing, collaboration agreements or government grants. The COVID-19 pandemic has resulted in ongoing volatility in financial markets. If our access to capital is restricted or associated borrowing costs increase as a result of developments in financial markets, including relating to the COVID-19 pandemic, our operations and financial condition could be adversely impacted. There is no assurance that the Company will be successful in obtaining sufficient funding on acceptable terms, if at all, and it could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could materially adversely affect its business prospects or its ability to continue operations.

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, revenue recognition, the accrual for clinical trial costs and other research and development expenses, and the valuation of share-based awards. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition, including expenses, manufacturing, clinical trials, research and development costs and employee-related amounts, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19 and the actions taken to contain it or treat COVID-19, as well as the economic impact on local, regional, national and international customers and markets. The Company has contemplated the impact of COVID-19 within its financial statements and is not aware of any specific event or circumstance that would require the Company to update estimates, judgments or revise the carrying value of any assets or liabilities. There may be changes to those estimates in future periods. 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.

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.

Consolidation

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.

In November 2019, the Company repurchased 100% of the minority investor's outstanding shares in Spero Gyrase, Inc. for $0.001 per share, and as a result, as of December 31, 2020 and 2019, the Company no longer reported a non-controlling interest. Additionally, effective as of January 1, 2020, the Company merged Spero Gyrase, Inc. with and into Spero, Therapeutics, 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. As of December 31, 2020, and 2019, the Company had no off-balance sheet risk such as foreign exchange contracts, option contracts, or other hedging arrangements.

Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents. Cash and cash equivalents include cash held in banks and money market instruments.

Marketable Securities

Marketable securities consist of investments in corporate obligations with original maturities greater than 90 days. The Company considers its 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 are included as a component of other income (expense), net based on the specific identification method. The Company evaluates debt securities with an unrealized loss to determine whether there may be a credit impairment. The Company also assesses its 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. Any credit impairments are recorded through an allowance account.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation and amortization expense are 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. The Company periodically evaluates whether events and circumstances have occurred that may warrant revision of the estimated useful life of property and equipment.

Leases

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

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company has elected not to recognize on the balance sheet leases with terms of one year or less. As of December 31, 2020, the Company had no short-term leases with terms of one year or less. Options to renew a lease are not included in the Company's initial lease term assessment unless there is reasonable certainty that the Company will renew. The Company monitors its plans to renew its material leases on a quarterly basis.

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

The Company has elected to account for lease and non-lease components together as a single lease component.

Other Assets

Other assets consist of long-term prepayments and deposits.

Impairment of Long-Lived Assets

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

Fair Value Measurements

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

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

The Company's cash equivalents 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.

Collaboration Agreements

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

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

Government Tax Incentives

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

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

Research and Development Costs

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

Clinical Trial and other Research Contract Costs and Accruals

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

Patent Costs

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

Share-Based Compensation

The Company measures all share-based awards granted to employees and directors based on the fair value on the date of grant using the Black-Scholes option-pricing model. Compensation expense of those awards is recognized over the requisite service period, which is generally the vesting period of the respective award. The Company records the expense for awards with service-based conditions using the straight-line method over the requisite service period, net of any actual forfeitures. The Company has also granted certain awards subject to performance-based vesting eligibility and a subsequent partial time-based vesting schedule. 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 that result from transactions and economic events other than those with shareholders. For the years ended December 31, 2020 and 2019, 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 years ended December 31, 2020 and 2019.

Net Loss per Share

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.

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.

In response to the COVID-19 pandemic, the Coronavirus Aid, Relief and Economic Security Act (CARES Act) was signed into law in March 2020. The CARES Act lifts certain deduction limitations originally imposed by the Tax Cuts and Jobs Act of 2017 (2017 Tax Act). Corporate taxpayers may carryback net operating losses (NOLs) originating during 2018 through 2020 for up to five years, which was not previously allowed under the 2017 Tax Act. The CARES Act also eliminates the 80% of taxable income limitations by allowing corporate entities to fully utilize NOL carryforwards to offset taxable income in 2018, 2019 or 2020. Taxpayers may generally deduct interest up to the sum of 50% of adjusted taxable income plus business interest income (30% limit under the 2017 Tax Act) for tax years beginning January 1, 2019 and 2020. The CARES Act allows taxpayers with alternative minimum tax credits to claim a refund in 2020 for the entire amount of the credits instead of recovering the credits through refunds over a period of years, as originally enacted by the 2017 Tax Act.

Recently Issued and Adopted Accounting Pronouncements

In June 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standard Update ("ASU") No 2016-13, *Financial Instruments – Credit Losses (Topic 326).* The Accounting Standards Codification 326, Financial Instruments- Credit Losses ("ASC 326") requires a financial asset measured at amortized cost basis to be presented at the net amount expected to be collected. Under ASU 2016-13, the Company is required to use a current expected credit loss ("CECL") model that immediately recognizes an estimate of credit losses that are expected to occur over the life of the financial instruments that are in the scope of the update, including trade receivables. The updated guidance also amends the previous other-than-temporary impairment model for available-for-sale debt securities by requiring the recognition of impairments related to credit losses through an allowance account and limits the amount of credit loss to the difference between a security's amortized cost basis and its fair value. In addition, the length of time a security has been in an unrealized loss position no longer impacts the determination of whether a credit loss exists. The Company adopted the guidance on January 1, 2020 with no impact. For available-for-sale securities, the updated guidance was applied prospectively.

In August 2018, the FASB issued ASU 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract (a consensus of the FASB Emerging Issues Task Force)* ("ASU 2018-15"). The amendments in ASU 2018-15 align the requirements for capitalizing implementation costs incurred in a hosting arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software (and hosting arrangements that include an internal-use software license). The Company adopted this standard as of January 1, 2020, on a prospective basis. The adoption did not have a material impact on the Company's consolidated financial statements.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement.* This standard modifies certain disclosure requirements on fair value measurements. This standard became effective for the Company on January 1, 2020 and did not have a material impact on its disclosures. For the new disclosures regarding our Level 3 instruments, please read Note 3, Fair Value Measurements, to these consolidated financial statements.

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606*. This standard makes targeted improvements for collaborative arrangements as follows:

- Clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue under Accounting Standards Codification (ASC) 606, Revenue from Contracts with Customers, when the collaborative arrangement participant is a customer in the context of a unit of account. In those situations, all the guidance in ASC 606 should be applied, including recognition, measurement, presentation and disclosure requirements;
- Adds unit-of-account guidance to ASC 808, Collaborative Arrangements, to align with the guidance in ASC 606 (that is, a distinct good or service) when an entity is assessing whether the collaborative arrangement or a part of the arrangement is within the scope of ASC 606; and
- Precludes a company from presenting transactions with collaborative arrangement participants that are not directly related to sales to third parties with revenue recognized under ASC 606 if the collaborative arrangement participant is not a customer.

This standard became effective for the Company on January 1, 2020 and did not have a material impact on its condensed consolidated financial statements and related disclosures.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*, amended guidance on the accounting and reporting of income taxes. The guidance is intended to simplify the accounting for income taxes by removing exceptions related to certain intraperiod tax allocations and deferred tax liabilities; clarifying guidance primarily related to evaluating the step-up tax basis for goodwill in a business combination; and reflecting enacted changes in tax laws or rates in the annual effective tax rate. The amended guidance is effective for interim and annual periods in 2021. Early adoption is permitted. The application of the amendments in the new guidance are to be applied on a retrospective basis, on a modified retrospective basis through a cumulative-effect adjustment to retained earnings or prospectively, depending on the amendment. The Company is currently evaluating the impact of adoption on its consolidated financial statements.

3. Fair Value Measurements and Marketable Securities

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, 2020 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ —	$ 73,488	$ —	$ 73,488
Commercial paper	—	5,998	—	5,998
Corporate bonds	—	3,006	—	3,006
Total cash equivalents	—	82,492	—	82,492
Marketable securities:				
Corporate bonds	—	13,221	—	13,221
Commercial paper	—	28,476	—	28,476
Total marketable securities	—	41,697	—	41,697
Total cash equivalents and marketable securities	$ —	$ 124,189	$ —	$ 124,189

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

Excluded from the tables above is cash of $2.7 million and $3.0 million as of December 31, 2020 and 2019, respectively. During the years ended December 31, 2020 and 2019, there were no transfers between Level 1, Level 2 and Level 3 categories.

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 Company evaluated debt securities with unrealized losses for any expected credit losses and determined unrealized losses on these securities were related to non-credit factors. Additionally, the Company currently does not intend to and is not required to sell these investments prior to an anticipated recovery in value.

The following table summarizes the gross unrealized gains and losses of the Company's marketable securities as of December 31, 2020 and 2019 (in thousands):

	December 31, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets:				
U.S. government securities	$ —	$ —	$ —	$ —
Corporate bonds	13,227	—	(6)	13,221
Commercial paper	28,476	—	—	28,476
	$ 41,703	$ —	$ (6)	$ 41,697

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

As of December 31, 2020 and 2019, all of the Company's marketable securities had remaining contractual maturity dates of one year or less from the consolidated balance sheet date.

Anti-Dilution Rights

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

In March 2016, in connection with the issuance of a non-controlling interest in its subsidiary, Spero Gyrase, Inc. ("Spero Gyrase"), to Biota Pharmaceuticals, Inc. (now Vaxart, Inc.) ("Vaxart"), the Company granted to Vaxart certain anti-dilution rights (see Note 10). In November 2019, the Company repurchased 100% of the minority investor's outstanding shares in Spero Gyrase, Inc. at a price per share of $0.001. As a result, as of December 31, 2020 and 2019, there are no anti-dilution rights outstanding. Additionally, effective as of January 1, 2020, the Company merged Spero Gyrase, Inc. with and into Spero, Therapeutics, Inc.

4. Property and Equipment, Net

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

	December 31,	
	2020	2019
Leasehold improvements	1,636	1,636
Manufacturing equipment	1,338	1,338
Computer software and equipment	$ 507	$ 438
Office furniture and equipment	424	364
Construction-in-progress	40	12
	3,945	3,788
Less: Accumulated depreciation and amortization	(2,276)	(1,515)
	$ 1,669	$ 2,273

Property and equipment additions during the year ended December 31, 2020 primarily related to office furniture and equipment and construction-in-progress related to the expansion of Company's leased office space (see Note 5). Property and equipment additions during the year ended December 31, 2019 primarily related to leasehold improvements previously in construction-in-progress. Depreciation and amortization expense was $0.8 million and $0.8 million for the years ended December 31, 2020 and 2019, respectively. During the year ended December 31, 2019, the Company wrote off $0.2 million of leased manufacturing equipment which the Company determined did not have any further use.

5. Leases

Operating Leases

In August 2015, the Company entered into an operating lease agreement with U.S. REIF Central Plaza Massachusetts, LLC (the "Landlord") with respect to its corporate headquarters located at 675 Massachusetts Avenue, Cambridge, Massachusetts (the "Original Lease"). The term of the Original Lease commenced in January 2016 and was scheduled to expire in December 2020. Under the terms of the Original Lease, the Company provided a security deposit of $0.2 million to the Landlord, which is included in long-term assets in the accompanying condensed consolidated balance sheets. The Original Lease provided for annual rent escalations as well as tenant incentives in the amount of $0.7 million, of which $0.3 million would be reimbursed to the Landlord over the initial term of the Original Lease.

On January 17, 2018, the Company entered into an amendment to the Original Lease (the "Amendment"). The Amendment made certain modifications to the Original Lease, including the addition of approximately 7,800 square feet of office space in the same building (the "Expansion Premises") and an extension of the expiration date of the Original Lease to seven years, or December 2025. The Amendment also provided for $0.4 million from the Landlord for leasehold improvements on the Expansion Premises.

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

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

On May 4, 2020, the Company entered into a third amendment to the Original Lease, as amended by the Second Amendment (the "Third Amendment"). The Third Amendment made certain modifications, including (i) amending the commencement date of the Second Expansion Premises with a term which began in August 2020, and (ii) an extension of the expiration date of all existing leases through July 2027.

For the years ended December 31, 2020 and 2019, the components of operating lease expense were as follows (in thousands):

Operating lease expense	Statement of Operations Location	December 31, 2020	December 31, 2019
Fixed operating lease expense	Research and development expense	$ 808	$ 601
	General and administrative expense	418	641
Variable operating lease expense	Research and development expense	89	56
	General and administrative expense	58	181
Total operating lease expense		$ 1,373	$ 1,479

Supplemental cash flow information related to the Company's operating leases for the years ended December 31, 2020 and 2019, was as follows (in thousands):

	December 31, 2020	December 31, 2019
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash flows from operating leases	$ 1,171	$ 1,234
Non-cash amounts resulting from the measurement of the lease liabilities:		
Right-of-use asset and lease obligation recorded upon commencement or amendment of lease agreements	2,626	1,038

Embedded Finance Leases

As part of our agreement with Meiji Seika Pharma Co. Ltd. ("Meiji"), the Company paid Meiji approximately $1.6 million during the three months ended December 31, 2018, related to fixed assets which will be used in manufacturing related activities at Meiji. The Company determined this equipment to be an embedded finance lease and has been capitalized as property and equipment in the consolidated balance sheet as of December 31, 2020 and 2019. As this equipment was fully paid in 2018, there is no corresponding lease liability as of December 31, 2020 or 2019.

The following table presents the lease balances within the consolidated balance sheet, weighted average remaining lease term, and the weighted average discount rates related to the Company's operating and finance leases as of December 31, 2020 and 2019 (in thousands, except for the weighted average remaining lease term and the weighted average discount rate):

Lease Assets and Liabilities	Classification	December 31, 2020	December 31, 2019
Assets			
Operating	Operating lease right-of-use assets	$ 7,114	$ 4,875
Financing	Property and equipment, net	736	1,004
Total leased assets		$ 7,850	$ 5,879
Liabilities			
Current			
Operating	Operating lease liabilities	$ 947	$ 928
Non-Current			
Operating	Non-current operating lease liabilities	6,891	4,617
Total lease liabilities		$ 7,838	$ 5,545
Weighted average remaining lease term (in years)		6.6	7.0
Weighted average discount rate		9.8%	10.3%

The following table presents the maturity of the Company's operating lease liabilities as of December 31, 2020 (in thousands):

Years Ending December 31,	
2021	$ 947
2022	1,662
2023	1,690
2024	1,718
2025	1,746
Thereafter	3,113
Total future minimum lease payments	10,876
Less imputed interest	(3,038)
Total operating lease liabilities	$ 7,838

6. Accrued Expenses and Other Current Liabilities

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

	December 31, 2020	December 31, 2019
Accrued external research and development expenses	$ 7,035	$ 17,746
Accrued payroll and related expenses	3,918	2,630
Accrued professional fees	1,066	803
Accrued other	222	409
	$ 12,241	$ 21,588

7. Equity Transactions

Underwritten Public Offering

On September 15, 2020, the Company completed an underwritten public offering of an aggregate of 4,785,000 shares of its common stock, and an aggregate of 3,215,000 shares of newly designated Series D Convertible Preferred Stock ("Series D Preferred Stock"). The price to the public in the offering was $10.00 per share with respect to the common stock and the Series D Preferred Stock. In addition, under the terms of the Underwriting Agreement, the Company granted the underwriters an option, exercisable for 30 days, to purchase up to 1,200,000 additional shares of common stock.

The offering closed on September 15, 2020 with an aggregate public offering price of $80.0 million. Aggregate net proceeds from the offering were $74.7 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company. Additionally, pursuant to the Underwriting Agreement, on October 1, 2020, the Company issued and sold 1,200,000 shares of common stock at the price of $10.00 per share pursuant to the underwriters' exercise of their option to purchase additional shares of common stock, resulting in additional net proceeds of approximately $11.2 million after deducting underwriting discounts and commissions.

Rights Offering

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

The Rights Offering was fully backstopped by certain affiliates of BVF Partners L.P. ("BVF"), which agreed to purchase, at a minimum, their respective as-converted pro rata share of the offered shares under the Rights Offering, plus an additional amount of Common Stock or Series C Preferred Shares that are not subscribed by other purchasers in the Rights Offering, for a total of up to $30.0 million.

At the closing of the rights offering on March 5, 2020, a total of 1,046,249 shares of the Company's common stock and 2,287 shares of Series C Preferred Stock were issued for aggregate gross proceeds of $30.0 million. The aggregate issuance costs related to the offering were $0.5 million. $20.6 million of the aggregate gross proceeds relates to the issuance of Series C and the associated issuance costs are $0.1 million.

Upon issuance, each share of Series C Preferred Stock included an embedded beneficial conversion feature. The beneficial conversion feature arose because the market price of the Company's common stock on the date of issuance of the Series C Preferred Stock was $9.22 per share as compared to an effective conversion price of the Series C Preferred Stock of $8.98 per share. As a result, the Company recorded the intrinsic value of the beneficial conversion feature of $0.5 million as a discount on the Series C Preferred Stock at issuance. Because the Series C Preferred Stock is immediately convertible upon issuance and does not include mandatory redemption provisions, the discount on the Series C Preferred Stock was immediately accreted.

8. Equity

Convertible Preferred Shares

Series A Convertible Preferred Shares

The Company has designated 2,220 of the 10,000,000 authorized shares of preferred stock as Series A Convertible Preferred Stock, or the Series A Preferred Stock

Each share of Series A 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 A 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 A Preferred Stock will receive a payment equal to $0.001 per share of Series A Preferred Stock before any proceeds are distributed to the holders of common stock. Shares of Series A Preferred Stock will generally have no voting rights, except as required by law and except that the consent of holders of a majority of the then outstanding Series A Preferred Stock will be required to amend the terms of the Series A Preferred Stock. As such, the Company has classified the Series A Preferred Stock within permanent equity in its consolidated balance sheet.

Series B Convertible Preferred Shares

The Company has designated 1,000 of the 10,000,000 authorized shares of preferred stock as Series B Convertible Preferred Stock, or the Series B 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 Series A Preferred Stock. Shares of Series B Preferred Stock will generally have no voting rights, except as required by law and except that the consent of holders of a majority of the then outstanding Series B Preferred Stock will be required to amend the terms of the Series B Preferred Stock. As such, the Company has classified the Series B Preferred Stock within permanent equity in its consolidated balance sheet.

Series C Convertible Preferred Shares

The Company has designated 3,333 of the 10,000,000 authorized shares of preferred stock as Series C Convertible Preferred Stock, or the Series C Preferred Stock

Each share of Series C 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 C 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 C Preferred Stock will receive a payment equal to $0.001 per share of Series C Preferred Stock before any proceeds are distributed to the holders of common stock and equal to any distributions to the holders of Series A Preferred Stock and Series B Preferred Stock. Shares of Series C Preferred Stock will generally have no voting rights, except as required by law and except that the consent of holders of a majority of the then outstanding Series C Preferred Stock will be required to amend the terms of the Series C Preferred Stock. As such, the Company has classified the Series C Preferred Stock within permanent equity in its consolidated balance sheet.

Series D Convertible Preferred Shares

The Company has designated 3,215,000 of the 10,000,000 authorized shares of preferred stock as Series D Convertible Preferred Stock, or the Series D Preferred Stock.

The shares of Series D Preferred Stock are convertible on a one-to-one basis into shares of common stock at any time at the option of the holder, provided that the holder will be prohibited from converting the Series D 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 D Preferred Stock will receive a payment equal to $0.001 per share of Series D Preferred Stock before any proceeds are distributed to the holders of common stock and equal to any distributions to the holders of Series A Preferred Stock, Series B Preferred Stock and Series C Preferred Stock. Shares of Series D Preferred Stock will generally have no voting rights, except as required by law and except that the consent of holders of a majority of the then outstanding Series D Preferred Stock will be required to amend the terms of the Series D Preferred Stock. As such, the Company has classified the Series D Preferred Stock within permanent equity in its consolidated balance sheet.

Common Stock

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 the Company 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. ("Cantor") 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.

The prospectus underlying the "at-the-market" offering program was terminated on September 9, 2020 in connection with the Company's underwritten public offering that was completed in September 2020. At such time, the Company had raised approximately $15.4 million in sales of its common stock under the "at-the-market" offering program, prior to deducting sales commissions, and had remaining available capacity of approximately $34.6 million. On November 13, 2020, the Company reinstated the "at-the-market" offering program with a capacity of up to $34.0 million by filing an updated prospectus.

Concurrently with the filing of this Annual Report on Form 10-K, the Company entered into a new sales agreement with Cantor and will be filing a new universal shelf registration statement on Form S-3, including an "at-the-market" prospectus with the SEC, which is further described elsewhere in this Annual Report on Form 10-K under "Item 9B. Other Events." The Company's existing sales agreement with Cantor will terminate automatically at such time as the SEC declares effective the Company's new universal shelf registration statement on Form S-3.

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

In June 2019, a holder of the Company's Series A Convertible Preferred stock elected to convert 500 shares into 500,000 shares of the Company's common stock, pursuant to such holder's rights under the certificate of designation for such Series A Convertible Preferred Stock. In December 2020, holders subsequently elected to convert the remaining 1,720 shares of Series A Preferred Stock into 1,720,000 shares of the Company's common stock, pursuant to such holder's rights under the certificate of designation for such Series A Preferred Stock.

In March 2020, at the closing of the rights offering, a total of 1,046,249 shares of the Company's common stock were issued with total gross proceeds of $9.4 million. The cost of offering incurred was $0.4 million.

In September 2020, at the closing of the underwritten public offering, a total of 4,785,000 shares of common stock and 3,215,000 shares of Series D Preferred Stock were issued with an aggregate public offering price of $80.0 million. Aggregate net proceeds from the offering were $74.7 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company. On October 1, 2020, the Company issued an additional 1,200,000 shares of its common stock pursuant to the underwriters' exercise, in full, of their option to purchase additional shares of common stock, resulting in additional net proceeds of approximately $11.2 million after deducting underwriting discounts and commissions.

During year ended December 31, 2020 the Company sold 993,870 shares of its common stock under the "at-the-market" offering sales agreement at an average price of approximately $13.66 per share for aggregate gross proceeds of approximately $13.6 million prior to deducting sales commissions.

9. Share-Based Compensation

2017 Stock Incentive Plan

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

On October 18, 2017, the Company's stockholders approved an amendment to the 2017 Plan, which became effective upon the completion of the Company's initial public offering, 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, 2020, there were 288,432 shares remaining available to be issued under the 2017 Plan.

2019 Equity Incentive Plan

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

In June 2020, the board of directors approved an increase of 700,000 shares of common stock for issuance under the 2019 Inducement Plan.

As of December 31, 2020, there were 481,500 shares remaining available to be issued under the 2019 Inducement Plan.

The following table summarizes stock option activity for all of our plans during 2020:

	2017 Plan	2019 Inducement Plan	Total Number of Stock Options
Outstanding as of December 31, 2019	2,798,128	171,300	2,969,428
Granted	821,828	392,700	1,214,528
Exercised	(319,433)	(5,000)	(324,433)
Forfeited or cancelled	(163,290)	(14,000)	(177,290)
Outstanding as of December 31, 2020	3,137,233	545,000	3,682,233

As of December 31, 2020, a total of 4,942,549 shares have been authorized and reserved for issuance under all equity plans and 769,932 shares were available for future issuance under such plans.

Performance-based awards

During 2019, the Company granted 100,000 options and 50,000 restricted stock units ("RSUs") containing the same performance-based vesting criteria. The 100,000 options are included in the table above but the 50,000 RSU's are excluded from the table. These options and RSUs (the "Performance Awards") are subject to performance-based vesting eligibility and a subsequent partial time-based vesting schedule. Specifically, the Performance Awards are eligible for vesting based on the achievement of performance criteria, each representing a 25% vesting opportunity if achieved within a specified time during the performance period (the "Performance Period"), and relating to (i) the release of tebipenem HBr top-line data; (ii) FDA acceptance of a tebipenem HBr New Drug Application; (iii) non-dilutive financing; and (iv) equity financing. Following the Performance Period, Performance Awards determined to be eligible for vesting as a result of achievement of the performance criteria will vest as follows: (a) 50% of the eligible award will vest immediately, and (b) the remaining eligible award will vest (i) in the case of options, in equal monthly installments ending two years after the Performance Period expiration, and (ii) in the case of RSUs, on such two year anniversary. During the year ended December 31, 2020, no compensation expense associated with performance-based awards was recognized as the performance conditions were not probable of achievement.

The following table summarizes the activity of options and RSUs under the 2017 Plan containing performance-based vesting criteria during the year ended December 31, 2020:

	Number of Performance Based Option Shares	Number of Performance Based RSU Shares
Outstanding as of December 31, 2019	84,146	40,750
Granted	-	-
Exercised	-	-
Forfeited or cancelled	(21,039)	(10,189)
Outstanding as of December 31, 2020	63,107	30,561

In January 2021, the Company cancelled the performance-based awards due to the non-achievement of the performance-based vesting criteria, and the awards were added back to the shares of common stock available for issuance under the 2017 Plan. None of the outstanding options had vested as of December 31, 2020.

Stock Option Valuation

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

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

	Year Ended December 31,	
	2020	2019
Risk-free interest rate	1.1%	2.4%
Expected term (in years)	6.2	6.3
Expected volatility	82.7%	75.2%
Expected dividend yield	0.0%	0.0%

The following table summarizes details regarding stock options granted under our equity incentive plans for the year ended December 31, 2020:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2019	2,969,428	$ 8.13	7.94	$ 6,689
Granted	1,214,528	10.94	—	—
Exercised	(324,433)	6.80	—	—
Forfeited or cancelled	(177,290)	9.94	—	—
Outstanding as of December 31, 2020	3,682,233	$ 9.10	7.84	$ 37,881
Outstanding as of December 31, 2020 - vested and expected to vest	3,682,233	$ 9.10	7.84	$ 37,881
Exercisable at December 31, 2020	1,771,383	$ 7.94	6.93	$ 20,286

The weighted average grant-date fair value of stock options granted during the year ended December 31, 2020 was $7.79 per share. The weighted average grant-date fair value of awards granted during the year ended December 31, 2019 was $5.62 per share. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2020 and 2019 was approximately $2.3 million and $0.4 million, respectively. The Company satisfies stock option exercises with newly issued shares of its common stock.

As of December 31, 2020, total unrecognized compensation cost related to unvested stock option grants was approximately $11.5 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,	
	2020	2019
Research and development expenses	$ 2,229	$ 1,580
General and administrative expenses	2,659	2,196
Total	$ 4,888	$ 3,776

10. Non-Controlling Interests

Spero Gyrase

In March 2016, the Company entered into an agreement with Aviragen and its affiliates in order to acquire certain intellectual property and know-how related to certain compounds. In connection with the transaction, the Company established Spero Gyrase, a Delaware corporation, and issued to Aviragen 200 common shares of Spero Gyrase with a fair value of $1.1 million, which represented a 20% equity ownership interest in Spero Gyrase. In addition, Spero Gyrase agreed to make future milestone and royalty payments in exchange for the intellectual property. The Company accounted for the acquisition of technology as an asset acquisition because it did not meet the definition of a business. The Company recorded the acquired technology as research and development expense in the consolidated statement of operations and comprehensive loss in the amount of $1.1 million, because the acquired technology had not reached commercial feasibility and had no alternative future use, and recorded a non-controlling interest in Spero Gyrase in a corresponding amount. In November 2019, the Company repurchased 100% of the minority investor’s outstanding shares in Spero Gyrase, Inc. at a price per share of $0.001. As a result, as of December 31, 2020 and 2019, the Company no longer reports a non-controlling interest. Additionally, effective as of January 1, 2020, the Company merged Spero Gyrase, Inc. with and into Spero, Therapeutics, Inc.

11. Income Taxes

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

During the years ended December 31, 2020 and 2019, 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,	
	2020	2019
Domestic	$ (77,671)	$ (62,623)
Foreign	(609)	1,698
Loss before income taxes	$ (78,280)	$ (60,925)

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,	
	2020	2019
Federal statutory income tax rate	(21.0)	(21.0)
Federal and state research and development tax credit	(3.2)	(3.0)
State taxes, net of federal benefit	(6.2)	(6.7)
Foreign rate differential	-	(0.8)
Nondeductible items	0.9	1.1
Increase in deferred tax asset valuation allowance	29.5	30.4
Effective income tax rate	—	—

Net deferred tax assets as of December 31, 2020 and 2019 consisted of the following (in thousands):

	December 31,	
	2020	2019
Net operating loss carryforwards	$ 63,612	$ 44,239
Research and development tax credit carryforwards	8,024	5,220
Other	3,403	2,521
Total deferred tax assets	75,039	51,980
Valuation allowance	(75,039)	(51,980)
Net deferred tax assets	$ —	$ —

As of December 31, 2020, the Company had U.S. federal and state net operating loss carryforwards of $228.1 million and $226.2 million, respectively, which may be available to offset future income tax liabilities. The federal NOLs of $73.0 million will expire at various dates from 2033 to 2037 and approximately $155.1 million can be carried forward indefinitely. The state NOLs begin to expire in 2033 and will expire at various dates through 2039. In addition, as of December 31, 2020, the Company had foreign net operating loss carryforwards of $10.7 million, which may be available to offset future income tax liabilities and do not expire. As of December 31, 2020, the Company also had federal and state research and development tax credit carryforwards of $6.7 million and $1.4 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2033 and 2028, respectively.

Utilization of the U.S. net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, and corresponding provisions of state law, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. Further, until a study is completed by the Company and any limitation is known, no amounts are being presented as an uncertain tax position.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the deferred tax assets as of December 31, 2020 and 2019. 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, 2020 and 2019 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,	
	2020	2019
Valuation allowance as of beginning of year	$ (51,980)	$ (34,141)
Decreases recorded as benefit to income tax provision	—	—
Increases recorded to income tax provision	(23,059)	(17,839)
Valuation allowance as of end of year	$ (75,039)	$ (51,980)

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2020 or 2019. 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, 2020 or 2019, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts had been recognized in the Company's statement of operations and comprehensive loss.

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

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

On December 22, 2017, former President Trump signed into law 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.

In response to the COVID-19 pandemic, the Coronavirus Aid, Relief and Economic Security Act ("CARES Act"), was signed into law in the United States in March 2020. The CARES Act adjusted a number of provisions of the tax code, including the calculation and eligibility of certain deductions and the treatment of net operating losses and tax credits. The enactment of the CARES Act did not result in any material adjustments to the Company's income tax provision for the year ended December 31, 2020, or to the Company's net deferred tax assets as of December 31, 2020.

12. Commitments and Contingencies

License Agreements

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

Operating Leases

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

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not aware of any claims under indemnification arrangements that 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, 2020 or 2019.

Legal Proceedings

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

13. Government Contracts

BARDA

In July 2018, the Company was awarded a contract from Biomedical Advanced Research and Development Authority ("BARDA") of up to $44.2 million to develop tebipenem HBr for the treatment of complicated urinary tract infections ("cUTI") caused by antibiotic resistant Gram-negative bacteria and for assessment against biodefense pathogens. The award committed initial funding of $15.7 million over a three-year base period from July 1, 2018 to June 30, 2021 for cUTI development activities. In May 2019, the contract was modified to include additional funding of approximately $2.5 million for development of tebipenem HBr, increasing the amount of the initial committed funding from $15.7 million to approximately $18.2 million and increasing the overall potential award to $46.8 million. In January 2020, BARDA exercised its first contract option for additional committed funding of $15.9 million, increasing the total committed funding to $34.1 million and extended the period of performance through November 1, 2021. The balance of the award is subject to BARDA exercising a second option which would entail funding of $12.7 million and is exercisable by BARDA subject to, among other things, satisfactory progress and results from the biodefense studies described below.

As part of an inter-agency collaboration between BARDA and the Defense Threat Reduction Agency ("DTRA"), a series of studies to assess the efficacy of tebipenem HBr in the treatment of infections caused by biodefense threats such as anthrax, plague and melioidosis will be conducted under the direction of Spero. The FDA requires data from a human pneumonic disease as supportive evidence of human efficacy when developing an antibiotic to treat a pulmonary biothreat infection under 21 CFR 314.600, "The Animal Rule," the scope of which the BARDA award includes the assessment of tebipenem HBr levels in the lung of healthy volunteers as well as a proof of concept clinical trial in pneumonia patients. DTRA provides up to $10.0 million, in addition to the total potential award from BARDA, to cover the cost of the nonclinical biodefense aspects of the collaborative program for tebipenem HBr. Together, BARDA and DTRA will provide up to $56.8 million in total funding for the clinical development and biodefense assessment of tebipenem HBr, of which $12.7 million is subject to the exercise of options by BARDA and Spero's achievement of specified milestones.

During the years ended December 31, 2020 and 2019, the Company recognized $7.9 million and $12.1 million of revenue under this agreement, respectively.

U.S. Department of Defense

On July 1, 2019, the Company received a $5.9 million award from the DoD Congressionally Directed Medical Research Programs ("CDMRP") Joint Warfighter Medical Research Program. The funding will support the further clinical development of SPR206. The award commits non-dilutive funding of $5.9 million over a four-year period to cover the costs of select Phase 1 pharmacology studies, a 28-day GLP non-human primate toxicology study, and microbiological surveillance studies that would be required for a potential New Drug Application, or NDA, submission with the U.S. Food and Drug Administration for SPR206. During the years ended December 31, 2020 and 2019, the Company recognized $0.4 million and less than $0.1 million in revenue under this agreement, respectively.

In September 2016, the Company was awarded a cooperative agreement from the Peer Reviewed Medical Research Program with the DoD to further develop anti-infective agents to combat Gram-negative bacteria. The agreement was initially structured as a single, two-year $1.5 million award through September 2018. The performance period was extended through September 29, 2019. The Company was eligible for the full funding from the DoD, as there were no options to be exercised at a later date. The DoD funding supported next-generation potentiator discovery and screening of SPR741 and SPR206. The Company and the DoD concluded the agreement at the end of the period of performance in September 2019. Company did not recognize any revenue under this agreement during the year ended December 31, 2020 and recognized $0.2 million in revenue under this agreement, during the year ended December 31, 2019.

NIAID

In February 2017, the Company was awarded a grant from the U.S. National Institute of Allergy and Infectious Diseases, or NIAID, under its Small Business Innovation Research program, over a two-year period from March 1, 2017 to February 28, 2019 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 was structured as a 12-month $0.6 million base period and a $0.4 million option period. Through December 31, 2017, only the base period funds were committed. In February 2018 NIAID exercised the $0.4 million 12-month option period. In January 2019, the period of performance for this award was extended for an additional 12-month period. During the years ended December 31, 2020 and 2019, the Company recognized less than $0.1 million and $0.1 million of revenue under this agreement, respectively, before concluding the grant with NIAID.

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 novate the then CAI-held NIAID contract to Spero, which was finalized in December 2017. The NIAID contract provides for development funding of up to $6.5 million over a base period and three option periods. As of December 31, 2020, funding for the base period and the first two option periods totaling $5.9 million have been committed. As part of the agreement, Spero was obligated to pay PBB a percentage of funds received from NIAID up to a maximum of $1.3 million, which was fulfilled as of December 31, 2020. During the years ended December 31, 2020 and 2019, the Company recognized $0.7 million and $1.0 million in revenue under this agreement, respectively.

14. License, Collaboration and Service Agreements

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

Vaxart (formerly Aviragen) License Agreement

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

Cantab License Agreements

Under the Cantab Agreements, the Company is obligated to make milestone payments of up to $5.8 million upon the achievement of specified clinical and regulatory milestones and a payment of £5.0 million ($6.8 million and $6.6 million as of December 31, 2020 and 2019, 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, 2020, the Company did not record any 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 $80.2 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, 2020, the Company paid and recorded $0.9 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 future milestone payments of up to $2.0 million upon the achievement of specified clinical and regulatory milestones, to pay royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement and to pay Meiji a low double-digit percentage of any sublicense fees received by the Company up to $7.5 million. In October 2017, the Company paid a $1.0 million milestone payment to Meiji upon the enrollment of the first patient in the Company's Phase 1 clinical trial of tebipenem HBr. The payment was recorded as research and development expense in the statement of operations and comprehensive loss for the year ended December 31, 2017. The Company paid Meiji approximately $1.6 million during the fourth quarter of 2018 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, 2020.

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

Northern License Agreement

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

Everest Medicines License Agreement

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

Under the terms of the Original Everest License Agreement and the Everest License Amendment, the Company received an upfront payment of $3.0 million that was recognized in the first quarter of 2019, comprised of a $2.0 million payment to license SPR206 and $1.0 million for the exclusive option to negotiate a license to develop SPR741. The Company also received a milestone payment of $2.0 million in the fourth quarter of 2020 upon completion and delivery of the results of a clinical study. The Company will receive future milestones of up to $1.5 million if the Company chooses to complete a future clinical study. On January 15, 2021, the Company entered into an amended and restated license agreement ("the Amended Everest License Agreement") with Everest and Potentiator, which amended and restated in its entirety the Original Everest License Agreement. The Amended Everest License Agreement modifies the dates and values of certain milestone events related to development and commercialization of SPR206. Everest will be now be making more significant investments in the development of SPR206 beyond what was contemplated at the

time of the Original Everest License Agreement. The Original Everest License Agreement provided that the Company could receive up to $59.5 million upon achievement of certain milestones. The Amended Everest License Agreement provides that the Company may receive up to $38.0 million upon achievement of certain milestones, of which $2.0 million has been received to date. In addition, under the Amended Everest License Agreement, the Company assigned patents in the Territory to Everest, rather than licensing such patents to Everest, and the option related to SPR741 and the related provisions have been removed. Under the terms of the Amended Everest License Agreement, the Company is also entitled to receive high single-digit to low double-digit royalties on net sales, if any, of Licensed Products in the Territory following regulatory approval of SPR206. Everest has the right to sublicense to affiliates and third parties in the Territory.

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

Unless earlier terminated due to certain material breaches of the contract, or otherwise, the Amended Everest License Agreement will expire on a jurisdiction-by-jurisdiction and Licensed Product-by-Licensed Product basis upon 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 Amended Everest License Agreement may be terminated in its entirety by Everest upon 90 or 180 days' prior written notice, depending on the stage of development of the initial Licensed Product.

Accounting Analysis and Revenue Recognition

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

Based on that evaluation, the Company identified three performance obligations, as presented below. The transaction price to be allocated to the identified performance obligations was determined to be $5.0 million consisting of: (i) the license upfront fee of $2.0 million, (ii) the $1.0 million exclusive option to negotiate a license to develop SPR741, and (iii) research and development services related to a milestone of $2.0 million for which the achievement of the milestone was determined "most likely," and that it was probable a significant reversal in the amount of cumulative revenue recognized would not occur. This milestone was achieved as of December 31, 2020. The additional clinical study that is at the Company's discretion to perform is considered a marketing offering and therefore not included in the assessment at contract inception. The Company determined that the license was distinct from the exclusive option for SPR741 and the research and development services. The following table shows the performance obligations, along with their SSP and the transaction price allocated to those obligations (in thousands):

Performance Obligations	Standalone Selling Price	Transaction Price Allocated	Recognition Method
License and know-how transfer (1)	$ 9,858	$ 3,553	Fully satisfied; recognized upon delivery of the license
Exclusive option on SPR741	400	144	Recognized in Q4 2019 upon the return of the IP rights to Northern
Research and development services (2)	3,614	1,303	Recognized over time as services are delivered through the completion date, and fully recognized as of December 31, 2020.
		$ 5,000	

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

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

During the year ended December 31, 2020, the Company recognized $0.3 million of revenue related to this agreement. As of December 31, 2020, the aggregate amount of the transaction price was fully allocated to satisfied performance obligations, the Company had delivered the Clinical Study Report covering the SAD/MAD Phase 1 Clinical Trial of SPR206 and pursuant to the Original Everest License Agreement, Everest paid the Company the $2.0 million milestone.

Gates MRI

In June 2019, the Company entered into a collaboration with Gates MRI to develop SPR720 for the treatment of lung infections caused by Mycobacterium tuberculosis. In furtherance of the Gates MRI's charitable purposes, the Company also granted to Gates MRI a no-cost, exclusive license to develop, manufacture and commercialize SPR720 for the treatment of tuberculosis ("TB") in low- and middle- income countries. The Gates MRI is responsible for formulating and funding its own research plan for the development of SPR720 for TB. As such, Gates MRI will conduct and fund preclinical and clinical studies for the development of SPR720 against TB. In addition, Gates MRI and the Company will jointly design and manage certain collaborative research activities, which the Company will perform and which will be funded by the Gates MRI. Due to the cost-funded nature of the payments and the Company's assessment that it does not have a vendor/customer relationship with the Gates MRI, the Company will recognize the funding received under the agreement as a reduction to the research and development expenses incurred, as the related expenses are incurred. During the years ended December 31, 2020 and 2019, the Company recorded $2.1 million and $1.7 million, respectively, as a reduction to research and development expense related to activities funded by Gates MRI.

Savior Service Agreement

In November 2018, the Company entered into a service agreement with Savior Lifetec Corporation ("Savior") to perform technology transfer, process development, analytical method development and testing and formulation development for tebipenem HBr. Per the terms of the agreement, the Company paid Savior a non-refundable supervision fee of approximately $2.0 million to manage the buildout of a commercial manufacturing facility. The supervision fee is classified as a prepaid asset on the Company's balance sheet and is being amortized over a service period of approximately 34 months. The Company has paid Savior an additional $5.1 million for facility build out costs, which is classified as a long-term asset on the Company's balance sheet as of December 31, 2020.

15. Australia Research and Development Tax Incentive

The Australian government has established a research and development tax incentive to encourage industry investment in research and development, which is available to companies incorporated under Australian law that have core research and development activities. In September 2016, the Company established Spero Potentiator Australia Pty Limited to carry out certain research and development activities. As this subsidiary meets the eligibility requirements of the Australian tax law, it is eligible to receive a 43.5% tax incentive for qualified research and development activities. For the years ended December 31, 2020 and 2019, $0.3 million and $0.4 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, 2020 and 2019, the Company's tax incentive receivables from the Australian government totaled $1.2 million and $0.8 million, respectively.

16. Net Loss per Share

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

	Year Ended December 31,	
	2020	2019
Numerator:		
Net loss	$ (78,280)	$ (60,925)
Deemed Dividend	(549)	-
Net loss attributable to common stockholders	$ (78,829)	$ (60,925)
Denominator:		
Weighted average common shares outstanding, basic and diluted	22,386,122	18,160,525
Net loss per share, basic and diluted	$ (3.52)	$ (3.35)

The net loss applicable to common stockholders for the year ended December 31, 2020 did not equal net loss due to the accretion of the beneficial conversion feature of Series C Preferred Stock in the amount of $0.5 million. The beneficial conversion feature was initially recorded as a discount on the Series C Preferred Stock with a corresponding amount recorded to Additional Paid-in Capital. The discount on the Series C Preferred Stock was then immediately written off as a deemed dividend as the Series C Preferred Stock does not have a stated redemption date and is immediately convertible at the option of the holder.

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

	Year Ended December 31,	
	2020	2019
Options to purchase common stock	3,682,233	2,969,428
Unvested restricted stock units	30,561	40,750
Series A convertible preferred stock (as converted to common shares)	—	1,720,000
Series B convertible preferred stock (as converted to common shares)	1,000,000	1,000,000
Series C convertible preferred stock (as converted to common shares)	2,287,000	—
Series D convertible preferred stock (as converted to common shares)	3,215,000	—
Total	10,214,794	5,730,178

17. Retirement Plan

The Company has a defined-contribution plan under Section 401(k) of the Internal Revenue Code (the “401(k) Plan”). The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pre-tax basis. As currently established, the Company is not required to make any contributions to the 401(k) Plan. The Company made matching contributions to the 401(k) Plan of $0.3 million and $0.2 million during the years ended December 31, 2020 and 2019, respectively.

18. Subsequent Events

On January 15, 2021, the Company entered into an amended and restated license agreement, or the Amended Everest License Agreement, with Everest and Potentiator, which amended and restated in its entirety the Original Everest License Agreement. The Amended Everest License Agreement provides for Spero to assign country-specific patents (in the Everest territory) to Everest as opposed to licensing them, adjusts diligence milestone dates to reflect updated clinical development plans and adjusts the value of potential development and sales milestones from $55.0 million to $34.5 million. Everest will share all Everest-funded data with the Company for use in its future regulatory submissions.

On February 5, 2021, the Company announced that the FDA informed Spero that a clinical hold had been placed on its Phase 2a clinical trial of SPR720, following the Company's notification to the FDA of its decision to pause dosing in its ongoing Phase 2a clinical trial of SPR720 as a precautionary measure related to events in its ongoing animal toxicology study of SPR720. The decision to implement the pause was made based on a recommendation from the Company's Safety Review Board, or SRB, following review of data from an ongoing toxicology study of SPR720 in adult non-human primates in which mortalities with inconclusive causality to treatment were observed. The animal study is being conducted to assess the potential toxicity of SPR720. A concurrent study of SPR720 in rats is proceeding uneventfully. These studies are meant to support longer-term treatment with SPR720 beyond the 28 days currently supported by IND-enabling toxicology studies. No serious adverse events have been observed in any human study participants.

Subsequent to receiving verbal notification from the FDA of the clinical hold, the Company received a formal clinical hold letter in which the FDA has requested additional information from the non-human primate trial, including a study report. The Company has decided to discontinue the Phase 2a clinical trial at this time to best facilitate future potential adjustments to the protocol based on FDA feedback and to avoid incurring costs associated with the trial while on clinical hold. The Company is continuing to work with the FDA to evaluate the findings and determine the further development pathway for the SPR720 clinical program.

With respect to its "at-the-market" program, on March 11, 2021, the Company entered into a new sales agreement with Cantor relating to sales, from time to time, of the Company's common stock up to an aggregate of $75.0 million. The Company will be filing a new universal shelf registration statement on Form S-3, including an "at-the-market" prospectus with the SEC concurrently with the filing of this Annual Report on Form 10-K.

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, 2020. 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, 2020, 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, 2020.

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, 2020 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

With respect to our "at-the-market" program, on March 11, 2021, we entered into a new sales agreement with Cantor relating to sales, from time to time, of the Company's common stock up to an aggregate of $75.0 million. We will also file a new universal shelf registration statement on Form S-3, including an "at the market" prospectus relating to the foregoing, with the SEC after the filing of this Annual Report on Form 10-K. Prior to the effectiveness of our new universal shelf registration statement on Form S-3, we intend to file an Amendment to this Annual Report on Form 10-K to present the information required by Part III of Form 10-K. Our existing sales agreement with Cantor, dated December 3, 2018, will terminate automatically at such time as the SEC declares effective our new universal shelf registration statement on Form S-3.

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 2021 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 2021 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 2021 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 2021 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 2021 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
3.5	Certificate of Designation of Preferences, Rights and Limitations of Series C Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	2/28/2020	001-38266
3.6	Certificate of Designation of Preferences, Rights and Limitations of Series D Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	9/14/2020	001-38266
4.1	Form of Common Stock Certificate		Form S-1 (Exhibit 4.1)	10/6/2017	333-220858
4.2	Investors' Rights Agreement, dated as of June 30, 2017, by and between the Registrant and the other parties thereto		Form S-1 (Exhibit 4.2)	10/6/2017	333-220858
4.3	Description of Registrant's Securities		Form 10-K (Exhibit 4.3)	3/16/2020	001-38266
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, as amended		Form 10-Q (Exhibit 10.1)	8/6/2020	001-38266
10.4#	Form of Stock Option Agreement under the 2019 Inducement Equity Incentive Plan, as amended		Form 10-Q (Exhibit 10.2)	8/6/2020	001-38266
10.5#	Form of Director and Officer Indemnification Agreement		Form S-1 (Exhibit 10.4)	10/6/2017	333-220858
10.6#	Non-Employee Director Compensation Policy, as amended		Form 10-K (Exhibit 10.6)	3/16/2020	001-38266

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 December 9, 2020, by and between the Registrant and Satyavrat Shukla	X			
10.9#	Amended and Restated Employment Agreement, dated April 22, 2020, by and between the Registrant and Thomas Parr Jr., Ph.D.		Form 10-Q (Exhibit 10.3)	8/6/2020	001-38266
10.10#	Employment Agreement, dated October 20, 2017, by and between the Registrant and Cristina Larkin		Form S-1/A (Exhibit 10.8)	10/23/2017	333-220858
10.11#	Employment Agreement, dated December 13, 2017, by and between the Registrant and David Melnick, M.D.		Form 10-K (Exhibit 10.9)	4/2/2018	001-38266
10.12#	Employment Agreement, dated January 1, 2020, by and between the Registrant and Timothy Keutzer		Form 10-K (Exhibit 10.12)	3/16/2020	001-38266
10.13#	Employment Agreement, dated November 6, 2020, by and between the Registrant and Tamara Joseph	X			
10.14#	Consulting Agreement, dated April 18, 2019, by and between the Registrant and David P. Southwell		Form 10-K (Exhibit 10.13)	3/16/2020	001-38266
10.15#	Consulting Agreement, dated November 4, 2019, by and between the Registrant and Danforth Advisors, LLC		Form 10-Q (Exhibit 10.1)	5/8/2020	001-38266
10.16#	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
10.17	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
10.18	Second Amendment to Lease Agreement, dated December 16, 2019, by and between the Registrant and U.S. REIF Central Plaza Massachusetts, LLC		Form 8-K (Exhibit 99.1)	12/19/2019	001-38266
10.19	Third Amendment to Lease Agreement, dated May 4, 2020, by and between the Registrant and U.S. REIF Central Plaza Massachusetts, LLC		Form 10-Q (Exhibit 10.4)	8/6/2020	001-38266
10.20	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
10.21†	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
10.22†	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
10.23†	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

10.24†	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
10.25††	Amended and Restated License Agreement, dated January 15, 2021, by and between the Registrant and Everest Medicines II Limited	X			
10.26	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
10.27	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
10.28	Controlled Equity Offering Sales Agreement, dated March 11, 2021, by and between the Registrant and Cantor Fitzgerald & Co.	X			
10.29	Securities Purchase Agreement, dated June 12, 2019, by and between the Registrant and Novo Holdings A/S		Form 10-Q (Exhibit 10.1)	8/8/2019	001-38266
10.30	Form of Proprietary Information and Inventions Assignment Agreement		Form S-1/A (Exhibit 10.17)	10/23/2017	333-220858
16.1	Letter of KPMG LLP, dated August 25, 2017, regarding changes in the Registrant's certifying accountants		Form S-1 (Exhibit 16.1)	10/6/2017	333-220858
21.1	List of Subsidiaries of the Registrant		Form 10-K (Exhibit 21.1)	3/16/2020	001-38266
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*	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, by Principal Executive Officer and Principal Financial Officer	X			

101.INS	XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document	X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	X

† Confidential treatment received as to portions of the exhibit. Confidential materials omitted and filed separately with the SEC.

†† Certain confidential portions of this Exhibit were omitted by means of marking such portions with brackets ("[***]") because the identified confidential portions (i) are not material and (ii) would be competitively harmful if publicly disclosed.

Management contract or compensatory plan.

* The certification attached as Exhibit 32 that accompanies this Annual Report on Form 10-K is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Spero Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

Item 16. Form 10-K Summary.

None.

SIGNATURES

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

SPERO THERAPEUTICS, INC.

Date: March 11, 2021

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 Sath Shukla his true and lawful attorney-in-fact and agent, with full power of substitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

IN WITNESS WHEREOF, each of the undersigned has executed this Power of Attorney as of the date indicated opposite his name.

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

Name	Title	Date
/s/ Ankit Mahadevia, M.D. Ankit Mahadevia, M.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 11, 2021
/s/ Sath Shukla Sath Shukla	Chief Financial Officer and Treasurer *(Principal Financial Officer and Principal Accounting Officer)*	March 11, 2021
/s/ Milind Deshpande, Ph.D. Milind Deshpande, Ph.D.	Director	March 11, 2021
/s/ Jean-François Formela, M.D. Jean-François Formela, M.D.	Director	March 11, 2021
/s/ Scott Jackson Scott Jackson	Director	March 11, 2021
/s/ John C. Pottage, M.D. John C. Pottage, M.D.	Director	March 11, 2021
/s/ Cynthia Smith Cynthia Smith	Director	March 11, 2021
/s/ Frank E. Thomas Frank E. Thomas	Director	March 11, 2021
/s/ Patrick Vink, M.D. Patrick Vink, M.D.	Director	March 11, 2021

EXECUTIVE EMPLOYMENT AGREEMENT

This Executive Employment Agreement (this "Agreement") is made and entered into this 9th day of December, 2020 (the "Effective Date") by and between Spero Therapeutics, Inc., a Delaware corporation ("Company"), and Satyavrat Shukla ("Executive").

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

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

1. Roles and Duties. Subject to the terms and conditions of this Agreement, Company shall employ Executive as its Chief Financial Officer ("CFO") reporting to Company's Chief Executive Officer ("CEO"). The Executive shall have such duties and responsibilities as are reasonably determined by the Board of Directors ("Board") and are consistent with the duties customarily performed by a CFO of a similarly situated company in the United States. Executive accepts such employment upon the terms and conditions set forth herein, and agrees to perform such duties and discharge such responsibilities to the best of Executive's ability. During Executive's employment, Executive shall devote all of Executive's business time and energies to the business and affairs of Company. Notwithstanding the foregoing, nothing herein shall preclude Executive from (i) performing services for such other companies as Company may designate or permit; (ii) serving, with the prior written consent of the Board, which consent shall not be unreasonably withheld, as a member of the boards of directors or advisory boards (or their equivalents in the case of a non-corporate entity) of non-competing businesses or charitable, educational or civic organizations; (iii) engaging in charitable activities and community affairs; and (iv) managing Executive's personal investments and affairs; provided, however, that the activities set out in clauses (i), (ii), (iii) and (iv) shall be limited by Executive so as not to materially interfere, individually or in the aggregate, with the performance of Executive's duties and responsibilities hereunder.

2. Term of Employment.

(a) Term. Subject to the terms hereof, Executive's employment hereunder shall commence on January 4, 2021 (the "Start Date") and continue until terminated hereunder by either party (such term of employment referred to herein as the "Term").

(b) Termination. Notwithstanding anything else contained in this Agreement, Executive's employment hereunder shall terminate upon the earliest to occur of the following:

(i) Death. Immediately upon Executive's death;

(ii) Termination by Company.

(A) If because of Executive's Disability (as defined below in Section 2(c)), written notice by Company to Executive that Executive's

employment is being terminated as a result of Executive's Disability, which termination shall be effective on the date of such notice or such later date as specified in writing by Company;

(B) If for Cause (as defined below in Section 2(d)), written notice by Company to Executive that Executive's employment is being terminated for Cause, which termination shall be effective on the date of such notice or such later date as specified in writing by Company, provided that if prior to the effective date of such termination Executive has cured the circumstances giving rise to the Cause (if capable of being cured as provided in Section 2(d)), then such termination shall not be effective; or

(C) If by Company for reasons other than under Sections 2(b)(ii)(A) or (B), written notice by Company to Executive that Executive's employment is being terminated, which termination shall be effective thirty (30) days after the date of such notice.

(iii) Termination by Executive.

(A) If for Good Reason (as defined below in Section 2(e)), written notice by Executive to Company that Executive is terminating Executive's employment for Good Reason and that sets forth the factual basis supporting the alleged Good Reason, which termination shall be effective thirty (30) days after the date of such notice; provided that if prior to the effective date of such termination Company has cured the circumstances giving rise to the Good Reason if capable of being cured as provided in Section 2(e), then such termination shall not be effective; or

(B) If without Good Reason, written notice by Executive to Company that Executive is terminating Executive's employment, which termination shall be effective no fewer than sixty (60) days after the date of such notice unless waived, in whole or in part, by Company.

Notwithstanding anything in this Section 2(b), Company may at any point, under the conditions set forth in Section 2(b)(ii)(B), terminate Executive's employment for Cause prior to the effective date of any other termination contemplated hereunder; provided that if prior to the effective date of such for-Cause termination Executive has cured the circumstances giving rise to the Cause (if capable of being cured as provided in Section 2(d)), then such termination shall not be effective.

(c) Definition of "Disability". For purposes of this Agreement, "Disability" shall mean Executive's incapacity or inability to perform Executive's duties and responsibilities as contemplated herein by reason of a medically determinable mental or physical impairment for one hundred twenty (120) days or more within any one (1) year period (cumulative or consecutive), which impairment can reasonably be expected to result in death or can be expected to last for a continuous period of not less than six (6) months. The determination that Executive is disabled hereunder, if disputed by the parties, shall be resolved by a physician reasonably satisfactory to

Executive and Company, at Company's expense, and the determination of such physician shall be final and binding upon both Executive and Company. Executive hereby consents to such examination and consultation by a physician. Company shall keep all information it receives as a result of such inquiry and determination confidential and shall not use it for any purpose other than in connection with exercising its rights under this Agreement.

(d) Definition of "Cause". As used herein, "Cause" shall mean: (i) Executive's conviction of (A) a felony or (B) any misdemeanor involving moral turpitude, deceit, dishonesty or fraud; (ii) Executive's willful failure or refusal to comply with lawful directions of the CEO, which failure or refusal continues for more than thirty (30) days after written notice is given to Executive by the CEO, which notice sets forth in reasonable detail the nature of such failure or refusal; (iii) willful and material breach by Executive of a written Company policy applicable to Executive or Executive's covenants and/or obligations under this Agreement or the material breach of the Restrictive Covenant Agreement; and/or (iv) material misconduct by Executive that seriously discredits or damages Company or any of its affiliates. Except in the case of (ii) above, it is not necessary that the Company's finding of Cause occur prior to Executive's termination of service. If Company determines, subsequent to Executive's termination of service, that prior to Executive's termination Executive engaged in conduct which would constitute "Cause," (other than pursuant to (ii) above) then Executive shall have no right to any benefit or compensation under this Agreement.

(e) Definition of "Good Reason". As used herein, "Good Reason" shall mean: (i) relocation of Executive's principal business location to a location more than thirty (30) miles from Executive's then-current business location; (ii) a material diminution in Executive's duties, authority or responsibilities; (iii) a material reduction in Executive's Base Salary; or (iv) willful and material breach by Company of its covenants and/or obligations under this Agreement; provided that, in each of the foregoing clauses (i) through (iv) (A) Executive provides Company with written notice that Executive intends to terminate Executive's employment hereunder for one of the grounds set forth in this Section 2(e) within thirty (30) days of such ground occurring, (B) if such ground is capable of being cured, Company has failed to cure such ground within a period of thirty (30) days from the date of such written notice, and (C) Executive terminates by written notice Executive's employment within sixty-five (65) days from the date that Executive provides the notice contemplated by clause (A) of this Section 2(e). For purposes of clarification, the above-listed conditions shall apply separately to each occurrence of Good Reason, and failure to adhere to such conditions in the event of Good Reason shall not disqualify Executive from asserting Good Reason for any subsequent occurrence of Good Reason. In addition, Executive may terminate Executive's employment for Good Reason within one (1) year following a Change of Control (as defined below) if, after the Change of Control, Executive is not an executive of the parent company, provided that Executive's roles, responsibilities and scope of authority within the subsidiary are not comparable to Executive's roles, responsibilities and scope of authority with Company prior to the Change of Control. For purposes of this Agreement, "Good Reason" shall be interpreted in a manner, and limited to the extent necessary, so that it shall not cause adverse tax consequences for either party with respect to Section 409A ("Section 409A") of the Internal Revenue Code of 1986, as amended (the "Code") and any successor statute, regulation and guidance thereto.

3. Compensation.

(a) Base Salary. Commencing on the Start Date, Company shall pay Executive a base salary (the "Base Salary") at the annual rate of Four Hundred Twenty Five Thousand Dollars ($425,000.00). The Base Salary shall be payable in substantially equal periodic installments in accordance with Company's payroll practices as in effect from time to time. Company shall deduct from each such installment all amounts required to be deducted or withheld under applicable law or under any employee benefit plan in which Executive participates. The Board or an appropriate committee thereof shall, on an annual basis, review the Base Salary, which may be adjusted upward (but not downward) at Company's discretion.

(b) Annual Performance Bonus. Commencing with fiscal year 2021, Executive shall be eligible to receive an annual cash bonus (the "Annual Performance Bonus"), with the target amount of such Annual Performance Bonus equal to forty percent (40%) of Executive's Base Salary in the year to which the Annual Performance Bonus relates; provided that the actual amount of the Annual Performance Bonus may be greater or less than such target amount. The amount of the Annual Performance Bonus shall be determined by the Board or an appropriate committee thereof in its sole discretion, and shall be paid to Executive no later than March 15th of the calendar year immediately following the calendar year in which it was earned. Except as provided in Section 4, Executive must be employed by Company on the last day of the applicable fiscal year to which the Annual Performance Bonus relates in order to be eligible for, and to be deemed as having earned, such Annual Performance Bonus. Company shall deduct from the Annual Performance Bonus all amounts required to be deducted or withheld under applicable law or under any employee benefit plan in which Executive participates.

(c) Equity. As a material inducement to the Executive joining the Company, on the Start Date, the Company shall award Executive an inducement stock option to purchase 75,000 shares of the Company's common stock, subject to approval by the Board or an authorized delegate thereof (the "Inducement Option Grant"). The Inducement Option Grant shall be subject to the terms and conditions of the Company's 2019 Inducement Equity Incentive Plan, as amended, and the applicable option agreement between the Executive and the Company entered into pursuant thereto. The Inducement Option Grant is intended as an inducement grant under Nasdaq Rule 5635(c)(4) and shall not qualify as an incentive stock option. The exercise price of the stock options subject to the Inducement Option Grant shall be the closing price of the Company's common stock on the Nasdaq Stock Market on the Start Date. The Inducement Option Grant shall be evidenced in writing by, and subject to the terms of, a Company stock option agreement which shall specify vesting over four (4) years, 25% on the first anniversary of the Start Date with the balance to vest in equal monthly installments over the following 36 months, and exercise of vested options for up to ten (10) years except as otherwise provided in the stock option agreement. Commencing in fiscal year 2022, Executive shall be eligible to be considered for the grant of stock options and/or other equity-based awards commensurate with Executive's position and responsibilities. The amount, terms and conditions of any stock option or other equity-based award shall be determined by the Board or an appropriate committee thereof in its discretion and set forth in the applicable equity plan and other documents governing the award.

(d) Paid Time Off. In addition to standard paid holidays, Executive may take up to twenty (20) days of paid time off ("PTO") per year, to be scheduled so as not to materially

disrupt Company's operations, pursuant to the terms and conditions of Company policy and practices as applied to Company senior executives.

(e) Fringe Benefits. Executive shall be entitled to participate in all benefit/welfare plans and fringe benefits provided to Company senior executives. Executive understands that, except when prohibited by applicable law, Company's benefit plans and fringe benefits may be amended by Company from time to time in its sole discretion. The terms of any such benefits shall be governed by the applicable plan documents and Company policies in effect from time to time.

(f) Reimbursement of Expenses. Company shall reimburse Executive for all ordinary and reasonable out-of-pocket business expenses incurred by Executive in furtherance of Company's business in accordance with Company's policies with respect thereto as in effect from time to time. Executive must submit any request for reimbursement no later than ninety (90) days following the date that such business expense is incurred. All reimbursements provided under this Agreement shall be made or provided in accordance with the requirements of Section 409A including, where applicable, the requirement that (i) any reimbursement is for expenses incurred during Executive's lifetime (or during a shorter period of time specified in this Agreement); (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year; (iii) the reimbursement of an eligible expense shall be made no later than the last day of the calendar year following the year in which the expense is incurred; and (iv) the right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

(g) Indemnification. Executive shall be entitled to indemnification with respect to Executive's services provided hereunder pursuant to Delaware law, the terms and conditions of Company's certificate of incorporation and/or by-laws, and Company's standard indemnification agreement for directors and officers as executed by Company and Executive. Executive shall be entitled to coverage under the Company's Directors' and Officers' ("D&O") insurance policies that it may hold now or in the future to the same extent and in the same manner (i.e., subject to the same terms and conditions) that the Company's other executive officers are entitled to coverage under any of the Company's D&O insurance policies that it may have.

(h) Sign-On Bonus. Company shall pay Executive a sign-on bonus (the "Sign-On Bonus") in the amount of One Hundred Sixty Four Thousand Dollars ($164,000.00), on the first payroll date following the Start Date, provided that in the event that Executive resigns Executive's employment with Company without Good Reason or the Company terminates Executive for Cause within one (1) year following the Start Date, Executive shall repay Company the amount of the Sign-On Bonus to Company within fifteen (15) days of Executive's termination date. Company shall deduct from the Sign-On Bonus all amounts required to be deducted or withheld under applicable law or under any employee benefit plan in which Executive participates. Executive hereby acknowledges and agrees that any required repayment of the Sign-On Bonus may be deducted from payments to be made by Company to Executive upon termination, including from the Accrued Obligations.

(i) Forfeiture/Clawback. All compensation shall be subject to any forfeiture or clawback policy established by Company generally for senior executives from time to time and any other such policy required by applicable law.

4. Payments Upon Termination.

(a) Definition of Accrued Obligations. For purposes of this Agreement, "Accrued Obligations" means: (i) the portion of Executive's Base Salary that has accrued prior to any termination of Executive's employment with Company and has not yet been paid; (ii) any accrued but unused PTO pursuant to Company's standard policy and practices; and (iii) the amount of any expenses properly incurred by Executive on behalf of Company prior to any such termination and not yet reimbursed. Executive's entitlement to any other compensation or benefit under any plan of Company shall be governed by and determined in accordance with the terms of such plans, except as otherwise specified in this Agreement.

(b) Termination by Company for Cause. If Executive's employment hereunder is terminated by Company for Cause, then Company shall pay the Accrued Obligations to Executive promptly following the effective date of such termination and shall have no further obligations with respect to any benefit or compensation under this Agreement to Executive hereunder.

(c) Termination by Executive Without Good Reason. If Executive's employment hereunder is terminated by Executive without Good Reason, then Company shall pay the Accrued Obligations and any accrued and unpaid Annual Performance Bonus for the prior fiscal year to Executive promptly following the effective date of such termination, and shall have no further obligations with respect to any benefit or compensation under this Agreement to Executive hereunder.

(d) Termination as a Result of Executive's Disability or Death. If Executive's employment hereunder terminates as a result of Executive's Disability or death, promptly after such termination Company shall pay to Executive: (i) the Accrued Obligations; (ii) any accrued and unpaid Annual Performance Bonus for the prior fiscal year; and (iii) the Pro Rated Bonus (as defined below), and shall have no further obligations with respect to any benefit or compensation under this Agreement to Executive hereunder. As used in this Section 4, "Pro Rated Bonus" shall mean an amount in cash equal to the target of Annual Performance Bonus for which Executive would have been eligible with respect to the year in which termination of Executive's employment occurs multiplied by a fraction, the numerator of which is the number of days during which Executive is employed by Company during the year of termination and the denominator of which is 365.

(e) Termination by Company Without Cause or by Executive For Good Reason. In the event that Executive's employment is terminated by action of Company other than for Cause, or Executive terminates Executive's employment for Good Reason, then, in addition to the Accrued Obligations and any accrued and unpaid Annual Performance Bonus for the prior fiscal year, Executive shall receive the following, subject to the terms and conditions described in Section 4(g) (including Executive's execution of the Release (as defined herein)):

(i) Severance Payments. Continuation of payments in an amount equal to Executive's then-current Base Salary for a nine (9) month period, less all customary and required taxes and employment-related deductions, in accordance with Company's normal payroll practices (provided such payments shall be made

at least monthly), commencing on the first payroll date following the date on which the Release required by Section 4(g) becomes effective and non-revocable, but not after seventy (70) days following the effective date of termination from employment; provided, that if the 70th day falls in the calendar year following the year during which the termination or separation from service occurred, then the payments shall commence in such subsequent calendar year; provided further that if such payments commence in such subsequent year, the first such payment shall be a lump sum in an amount equal to the payments that would have come due since Employee's separation from service.

(ii) Pro Rata Bonus. Payment of the Pro Rated Bonus, paid to Executive no later than March 15 of the calendar year next preceding the year of termination of employment, after deduction of all amounts required to be deducted or withheld under applicable law.

(iii) Benefits Payments. Upon completion of appropriate forms and subject to applicable terms and conditions under the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended ("COBRA"), Company shall continue to provide Executive medical insurance coverage to the same extent that such insurance continues to be provided to similarly situated executives at the time of Executive's termination with the cost of the regular premium for such benefits shared in the same relative proportion by Company and Executive as in effect on the last day of employment (the "COBRA Payment"), until the earlier to occur of: (i) twelve (12) months following Executive's termination date, or (ii) the date Executive becomes eligible for medical benefits with another employer. Notwithstanding the foregoing, if Executive's COBRA Payment would cause the applicable group health plan to be discriminatory and, therefore, result in adverse tax consequences to Executive, Company shall, in lieu of the COBRA Payment, provide Executive with an equivalent monthly cash payment, minus deduction of all amounts required to be deducted or withheld under applicable law, for any period of time Executive is eligible to receive the COBRA Payment. Executive shall bear full responsibility for applying for COBRA continuation coverage and Company shall have no obligation to provide Executive such coverage if Executive fails to elect COBRA benefits in a timely fashion.

Payment of the above described severance payments and benefits are expressly conditioned on Executive's execution without revocation of the Release and return of Company property under Section 6.

(f) Termination by Company Without Cause or by Executive For Good Reason Following a Change of Control. In the event that a Change of Control (as defined below) occurs and within a period of one (1) year following the Change of Control, or ninety (90) days preceding the earlier to occur of a Change of Control or the execution of a definitive agreement the consummation of which would result in a Change of Control, Executive's employment is terminated other than for Cause, or Executive terminates Executive's employment for Good Reason, then, in addition to the Accrued Obligations and any accrued and unpaid Annual

Performance Bonus for the prior fiscal year, Executive shall receive the following, subject to the terms and conditions described in Section 4(g) (including Executive's execution of the Release):

(i) Lump Sum Severance Payment. Payment of a lump sum amount equal to twelve (12) months of Executive's then-current Base Salary plus the Pro Rated Bonus, less all customary and required taxes and employment-related deductions, paid on the first payroll date following the date on which the Release required by Paragraph 4(g) becomes effective and non-revocable, but not after seventy (70) days following the effective date of termination from employment.

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

(iii) Benefit Payments. Upon completion of appropriate forms and subject to applicable terms and conditions under COBRA, Company shall continue to provide Executive medical insurance coverage to the same extent that such insurance continues to be provided to similarly situated executives at the time of Executive's termination with the cost of the regular premium for such benefits shared in the same relative proportion by Company and Executive as in effect on the last day of employment, until the earlier to occur of: (i) twelve (12) months following Executive's termination date, or (ii) the date Executive becomes eligible for medical benefits with another employer. Notwithstanding the foregoing, if Executive's COBRA Payment would cause the applicable group health plan to be discriminatory and, therefore, result in adverse tax consequences to Executive, Company shall, in lieu of the COBRA Payment, provide Executive with an equivalent monthly cash payment, minus deduction of all amounts required to be deducted or withheld under applicable law, for any period of time Executive is eligible to receive the COBRA Payment. Executive shall bear full responsibility for applying for COBRA continuation coverage and Company shall have no obligation to provide Executive such coverage if Executive fails to elect COBRA benefits in a timely fashion.

Payment of the above described severance payments and benefits are expressly conditioned on Executive's execution without revocation of the Release and return of Company property under Section 6. In the event that Executive is eligible for the severance payments and benefits under this Section 4(f), Executive shall not be eligible for any of the severance payments and benefits as provided in Section 4(e).

As used herein, a "Change of Control" shall mean the occurrence of any of the following events: (i) Ownership. Any "Person" (as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended) becomes the "Beneficial Owner" (as defined in Rule 13d-3 under said Act), directly or indirectly, of securities of Company representing fifty percent (50%) or more of the total voting power represented by Company's then outstanding voting securities (excluding for this purpose any such voting securities held by Company, or any affiliate, parent or subsidiary of Company, or by any employee benefit plan of Company) pursuant to a transaction or a series of related transactions; or (ii) Merger/Sale of Assets. (A) A merger or consolidation of Company whether or not approved by the Board, other than a merger or consolidation which would result in the voting securities of Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or the parent of such corporation) at least fifty percent (50%) of the total voting power represented by the voting securities of Company or such surviving entity or parent of such corporation, as the case may be, outstanding immediately after such merger or consolidation; (B) or Company's stockholders approve an agreement for the sale or disposition by Company of all or substantially all of Company's assets; or (iii) Change in Board Composition. A change in the composition of the Board, as a result of which fewer than a majority of the directors are Incumbent Directors. "Incumbent Directors" shall mean directors who either (A) are directors of Company as of the date of this Agreement, or (B) are elected, or nominated for election, to the Board with the affirmative votes of at least a majority of the Incumbent Directors, or by a committee of the Board made up of at least a majority of the Incumbent Directors, at the time of such election or nomination (but shall not include an individual whose election or nomination is in connection with an actual or threatened proxy contest relating to the election of directors).

(g) Execution of Release of Claims. Company shall not be obligated to pay Executive any of the severance payments or benefits described in this Section 4 unless and until Executive has executed (without revocation) a release of claims as described below (the "Release"). The Release shall contain reasonable and customary provisions including a general release of claims against Company and its affiliated entities and each of their officers, directors and employees as well as mutual non-disparagement, non-competition, non-solicitation, confidentiality, cooperation and the like. The Release must be provided to Executive not later than fifteen (15) days following the effective date of termination of Executive's employment by Company and executed by Executive and returned to Company within sixty (60) days after such effective date. If Executive fails or refuses to return the Release within such 60-day period, Executive's severance payments and benefits to be paid hereunder shall be forfeited.

(h) No Other Payments or Benefits Owing. Except as expressly set forth herein, the payments and benefits set forth in this Section 4: (a) shall be the sole amounts owing to Executive upon termination of Executive's employment for the reasons set forth above, and Executive shall not be eligible for any other payments or other forms of compensation or benefits; (b) shall be the sole remedy, if any, available to Executive in the event that Executive brings any claim against Company relating to the termination of Executive's employment under this Agreement; and (c) shall not be subject to set-off by Company or any obligation on the part of Executive to mitigate or to offset compensation earned by Executive in other pursuits after termination of employment, other than as specified herein with respect to medical benefits provided by another employer.

5. Prohibited Competition and Solicitation. Executive expressly acknowledges that: (a) there are competitive and proprietary aspects of the business of Company; (b) during the course of Executive's employment, Company shall furnish, disclose or make available to Executive confidential and proprietary information and may provide Executive with unique and specialized training; (c) such Confidential Information and training have been developed and shall be developed by Company through the expenditure of substantial time, effort and money, and could be used by Executive to compete with Company; and (d) in the course of Executive's employment, Executive shall be introduced to customers and others with important relationships to Company, and any and all "goodwill" created through such introductions belongs exclusively to Company, including, but not limited to, any goodwill created as a result of direct or indirect contacts or relationships between Executive and any customers of Company. In light of the foregoing acknowledgements, and as a condition of employment hereunder, Executive hereby approves the Restrictive Covenant Agreement entered into on the date hereof as a binding obligation of the Executive, enforceable in accordance with its terms.

6. Property and Records. Upon the termination of Executive's employment hereunder for any reason or for no reason, or if Company otherwise requests, Executive shall: (a) return to Company all tangible business information and copies thereof (regardless how such Confidential Information or copies are maintained), and (b) deliver to Company any property of Company which may be in Executive's possession, including, but not limited to, Blackberry-type devices, smart phones, laptops, cell phones (the foregoing, "electronic devices"), products, materials, memoranda, notes, records, reports or other documents or photocopies of the same. Executive may retain copies of any exclusively personal data contained in or on Company-owned electronic devices returned to Company pursuant to the foregoing. The foregoing notwithstanding, Executive understands and agrees that Company property belongs exclusively to Company, it should be used for Company business, and Executive has no reasonable expectation of privacy on any Company property or with respect to any information stored thereon.

7. Cooperation. During and after Executive's employment, Executive shall fully cooperate with Company to the extent reasonable in the defense or prosecution of any claims or actions now in existence or which may be brought in the future against or on behalf of Company (other than claims directly or indirectly against Executive) which relate to events or occurrences that transpired while Executive was employed by Company. Executive's cooperation in connection with such claims or actions shall include, but not be limited to, being available to meet with counsel to prepare for discovery or trial and to act as a witness on behalf of Company at mutually convenient times. During and after Executive's employment, Executive also shall fully cooperate with Company to the extent reasonable in connection with any investigation or review of any federal, state or local regulatory authority as any such investigation or review relates to events or occurrences that transpired while Executive was employed by Company. Company shall reimburse Executive for any reasonable out-of-pocket expenses incurred in connection with the Executive's performance of obligations pursuant to this section. In addition, Company shall compensate Executive on an hourly basis, based on a rate commensurate with Executive's Base Salary in effect prior to termination, for time Executive spends in excess of 10 hours in any calendar quarter providing services to the Corporation after termination.

8. Code Sections 409A and 280G.

(a) In the event that the payments or benefits set forth in Section 4 of this Agreement constitute "non-qualified deferred compensation" subject to Section 409A, then the following conditions apply to such payments or benefits:

(i) Any termination of Executive's employment triggering payment of benefits under Section 4 must constitute a "separation from service" under Section 409A(a)(2)(A)(i) of the Code and Treas. Reg. §1.409A-1(h) before distribution of such benefits can commence. To the extent that the termination of Executive's employment does not constitute a separation of service under Section 409A(a)(2)(A)(i) of the Code and Treas. Reg. §1.409A-1(h) (as the result of further services that are reasonably anticipated to be provided by Executive to Company at the time Executive's employment terminates), any such payments under Section 4 that constitute deferred compensation under Section 409A shall be delayed until after the date of a subsequent event constituting a separation of service under Section 409A(a)(2)(A)(i) of the Code and Treas. Reg. §1.409A-1(h). For purposes of clarification, this Section 8(a) shall not cause any forfeiture of benefits on Executive's part, but shall only act as a delay until such time as a "separation from service" occurs.

(ii) Notwithstanding any other provision with respect to the timing of payments under Section 4 if, at the time of Executive's termination, Executive is deemed to be a "specified employee" of Company (within the meaning of Section 409A(a)(2)(B)(i) of the Code), then limited only to the extent necessary to comply with the requirements of Section 409A, any payments to which Executive may become entitled under Section 4 which are subject to Section 409A (and not otherwise exempt from its application) shall be withheld until the first (1st) business day of the seventh (7th) month following the termination of Executive's employment, at which time Executive shall be paid an aggregate amount equal to the accumulated, but unpaid, payments otherwise due to Executive under the terms of Section 4.

(b) It is intended that each installment of the payments and benefits provided under Section 4 of this Agreement shall be treated as a separate "payment" for purposes of Section 409A. Neither Company nor Executive shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

(c) Notwithstanding any other provision of this Agreement to the contrary, this Agreement shall be interpreted and at all times administered in a manner that avoids the inclusion of compensation in income under Section 409A, or the payment of increased taxes, excise taxes or other penalties under Section 409A. The parties intend this Agreement to be in compliance with Section 409A. Executive acknowledges and agrees that Company does not guarantee the tax treatment or tax consequences associated with any payment or benefit arising under this Agreement, including but not limited to consequences related to Section 409A.

(d) If any payment or benefit Executive would receive under this Agreement, when combined with any other payment or benefit Executive receives pursuant to a Change of Control (for purposes of this section, a "Payment") would: (i) constitute a "parachute payment" within the meaning of Section 280G the Code; and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either: (A) the full amount of such Payment; or (B) such lesser amount (with cash payments being reduced before stock option compensation) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employments taxes, income taxes, and the Excise Tax, results in Executive's receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax. Notwithstanding the foregoing, if, prior to the closing of an initial public offering, any Payment can be exempt from the definition of "parachute payment" and the Excise Tax pursuant to the shareholder approval requirements described in Treas. Regs. § 1.280G-1, Q&A 6, the Company will, at the Executive's election (and subject to the Executive signing an appropriate waiver) seek shareholder approval to exempt such Payment from the definition of "parachute payment" and the Excise Tax.

9. General.

(a) Notices. Except as otherwise specifically provided herein, any notice required or permitted by this Agreement shall be in writing and shall be delivered as follows with notice deemed given as indicated: (i) by personal delivery when delivered personally; (ii) by overnight courier upon written verification of receipt; (iii) by telecopy or facsimile transmission upon acknowledgment of receipt of electronic transmission; or (iv) by certified or registered mail, return receipt requested, upon verification of receipt.

- Notices to Executive shall be sent to the last known address in Company's records or such other address as Executive may specify in writing.

- Notices to Company shall be sent to:

  Spero Therapeutics, Inc.
  675 Massachusetts Ave., 14th Floor
  Cambridge, MA 02139
  Attn: CEO

(b) Modifications and Amendments. The terms and provisions of this Agreement may be modified or amended only by written agreement executed by the parties hereto.

(c) Waivers and Consents. The terms and provisions of this Agreement may be waived, or consent for the departure therefrom granted, only by a written document executed by the party entitled to the benefits of such terms or provisions. No such waiver or consent shall be deemed to be or shall constitute a waiver or consent with respect to any other terms or provisions of this Agreement, whether or not similar. Each such waiver or consent shall be effective only in the specific instance and for the purpose for which it was given and shall not constitute a continuing waiver or consent.

(d) Assignment. Company may assign its rights and obligations hereunder to any person or entity that succeeds to all or substantially all of Company's business or that aspect of Company's business in which Executive is principally involved. Executive may not assign Executive's rights and obligations under this Agreement without the prior written consent of Company.

(e) Governing Law/Dispute Resolution. This Agreement and the rights and obligations of the parties hereunder shall be construed in accordance with and governed by the law of the Commonwealth of Massachusetts without giving effect to the conflict of law principles thereof. Any legal action or proceeding with respect to this Agreement shall be brought in the courts of the Commonwealth of Massachusetts or of the United States of America for the District of Massachusetts. By execution and delivery of this Agreement, each of the parties hereto accepts for itself and in respect of its property, generally and unconditionally, the non-exclusive jurisdiction of the aforesaid courts.

(f) Jury Waiver. ANY, ACTION, DEMAND, CLAIM, OR COUNTERCLAIM ARISING UNDER OR RELATING TO THIS AGREEMENT SHALL BE RESOLVED BY A JUDGE ALONE, AND EACH OF COMPANY AND EXECUTIVE WAIVES ANY RIGHT TO A JURY TRIAL THEREOF.

(g) Headings and Captions. The headings and captions of the various subdivisions of this Agreement are for convenience of reference only and shall in no way modify or affect the meaning or construction of any of the terms or provisions hereof.

(h) Entire Agreement. This Agreement, together with the other agreements specifically referenced herein, embodies the entire agreement and understanding between the parties hereto with respect to the subject matter hereof and supersedes all prior oral or written agreements and understandings relating to the subject matter hereof. No statement, representation, warranty, covenant or agreement of any kind not expressly set forth in this Agreement shall affect, or be used to interpret, change or restrict, the express terms and provisions of this Agreement.

(i) Counterparts. This Agreement may be executed in two or more counterparts, and by different parties hereto on separate counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. For all purposes a signature by fax shall be treated as an original.

[Signature Page to Follow]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first written above.

SATYAVRAT SHUKLA

/s/ Satyavrat Shukla
Signature

SPERO THERAPEUTICS, INC.

By: /s/ Ankit Mahadevia
Name: Ankit Mahadevia
Title: CEO

EXECUTIVE EMPLOYMENT AGREEMENT

This Executive Employment Agreement (this "Agreement") is made and entered into this 6th day of November, 2020 (the "Effective Date") by and between Spero Therapeutics, Inc., a Delaware corporation ("Company"), and Tamara Joseph ("Executive").

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

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

1. Roles and Duties. Subject to the terms and conditions of this Agreement, Company shall employ Executive as its Chief Legal Officer ("CLO") reporting to Company's Chief Executive Officer ("CEO"). The Executive shall have such duties and responsibilities as are reasonably determined by the Board of Directors ("Board") and are consistent with the duties customarily performed by a CLO of a similarly situated company in the United States. Executive accepts such employment upon the terms and conditions set forth herein, and agrees to perform such duties and discharge such responsibilities to the best of Executive's ability. During Executive's employment, Executive shall devote all of Executive's business time and energies to the business and affairs of Company. Notwithstanding the foregoing, nothing herein shall preclude Executive from: (i) providing consulting services to Millendo Therapeutics US, Inc., up to a maximum of five (5) hours per week, through January 31, 2021; (ii) performing services for such other companies as Company may designate or permit; (iii) serving on the board of directors of the non-profit organization Heluna Health and, with the prior written consent of the Board, which consent shall not be unreasonably withheld, otherwise serving as a member of the boards of directors or advisory boards (or their equivalents in the case of a non-corporate entity) of non-competing businesses or charitable, educational or civic organizations; (iv) engaging in charitable activities and community affairs; and (v) managing Executive's personal investments and affairs; provided, however, that the activities set out in clauses (i), (ii), (iii), (iv) and (v) shall be limited by Executive so as not to materially interfere, individually or in the aggregate, with the performance of Executive's duties and responsibilities hereunder..

2. Term of Employment.

(a) Term. Subject to the terms hereof, Executive's employment hereunder shall commence on December 2, 2020 (the "Start Date") and continue until terminated hereunder by either party (such term of employment referred to herein as the "Term").

(b) Termination. Notwithstanding anything else contained in this Agreement, Executive's employment hereunder shall terminate upon the earliest to occur of the following:

(i) Death. Immediately upon Executive's death;

(ii) Termination by Company.

(A) If because of Executive's Disability (as defined below in Section 2(c)), written notice by Company to Executive that Executive's employment is being terminated as a result of Executive's Disability, which termination shall be effective on the date of such notice or such later date as specified in writing by Company;

(B) If for Cause (as defined below in Section 2(d)), written notice by Company to Executive that Executive's employment is being terminated for Cause, which termination shall be effective on the date of such notice or such later date as specified in writing by Company, provided that if prior to the effective date of such termination Executive has cured the circumstances giving rise to the Cause (if capable of being cured as provided in Section 2(d)), then such termination shall not be effective; or

(C) If by Company for reasons other than under Sections 2(b)(ii)(A) or (B), written notice by Company to Executive that Executive's employment is being terminated, which termination shall be effective thirty (30) days after the date of such notice.

(iii) Termination by Executive.

(A) If for Good Reason (as defined below in Section 2(e)), written notice by Executive to Company that Executive is terminating Executive's employment for Good Reason and that sets forth the factual basis supporting the alleged Good Reason, which termination shall be effective thirty (30) days after the date of such notice; provided that if prior to the effective date of such termination Company has cured the circumstances giving rise to the Good Reason if capable of being cured as provided in Section 2(e), then such termination shall not be effective; or

(B) If without Good Reason, written notice by Executive to Company that Executive is terminating Executive's employment, which termination shall be effective no fewer than sixty (60) days after the date of such notice unless waived, in whole or in part, by Company.

Notwithstanding anything in this Section 2(b), Company may at any point, under the conditions set forth in Section 2(b)(ii)(B), terminate Executive's employment for Cause prior to the effective date of any other termination contemplated hereunder; provided that if prior to the effective date of such for-Cause termination Executive has cured the circumstances giving rise to the Cause (if capable of being cured as provided in Section 2(d)), then such termination shall not be effective.

(c) Definition of "Disability". For purposes of this Agreement, "Disability" shall mean Executive's incapacity or inability to perform Executive's duties and responsibilities as contemplated herein by reason of a medically determinable mental or physical impairment for one

hundred twenty (120) days or more within any one (1) year period (cumulative or consecutive), which impairment can reasonably be expected to result in death or can be expected to last for a continuous period of not less than six (6) months. The determination that Executive is disabled hereunder, if disputed by the parties, shall be resolved by a physician reasonably satisfactory to Executive and Company, at Company's expense, and the determination of such physician shall be final and binding upon both Executive and Company. Executive hereby consents to such examination and consultation by a physician. Company shall keep all information it receives as a result of such inquiry and determination confidential and shall not use it for any purpose other than in connection with exercising its rights under this Agreement.

(d) Definition of "Cause". As used herein, "Cause" shall mean: (i) Executive's conviction of (A) a felony or (B) any misdemeanor involving moral turpitude, deceit, dishonesty or fraud; (ii) Executive's willful failure or refusal to comply with lawful directions of the CEO, which failure or refusal continues for more than thirty (30) days after written notice is given to Executive by the CEO, which notice sets forth in reasonable detail the nature of such failure or refusal; (iii) willful and material breach by Executive of a written Company policy applicable to Executive or Executive's covenants and/or obligations under this Agreement or the material breach of the Restrictive Covenant Agreement; and/or (iv) material misconduct by Executive that seriously discredits or damages Company or any of its affiliates. Except in the case of (ii) above, it is not necessary that the Company's finding of Cause occur prior to Executive's termination of service. If Company determines, subsequent to Executive's termination of service, that prior to Executive's termination Executive engaged in conduct which would constitute "Cause," (other than pursuant to (ii) above) then Executive shall have no right to any benefit or compensation under this Agreement.

(e) Definition of "Good Reason". As used herein, "Good Reason" shall mean: (i) relocation of Executive's principal business location to a location more than thirty (30) miles from Executive's then-current business location; (ii) a material diminution in Executive's duties, authority or responsibilities; (iii) a material reduction in Executive's Base Salary; or (iv) willful and material breach by Company of its covenants and/or obligations under this Agreement; provided that, in each of the foregoing clauses (i) through (iv) (A) Executive provides Company with written notice that Executive intends to terminate Executive's employment hereunder for one of the grounds set forth in this Section 2(e) within thirty (30) days of such ground occurring, (B) if such ground is capable of being cured, Company has failed to cure such ground within a period of thirty (30) days from the date of such written notice, and (C) Executive terminates by written notice Executive's employment within sixty-five (65) days from the date that Executive provides the notice contemplated by clause (A) of this Section 2(e). For purposes of clarification, the above-listed conditions shall apply separately to each occurrence of Good Reason, and failure to adhere to such conditions in the event of Good Reason shall not disqualify Executive from asserting Good Reason for any subsequent occurrence of Good Reason. In addition, Executive may terminate Executive's employment for Good Reason within one (1) year following a Change of Control (as defined below) if, after the Change of Control, Executive is not an executive of the parent company, provided that Executive's roles, responsibilities and scope of authority within the subsidiary are not comparable to Executive's roles, responsibilities and scope of authority with Company prior to the Change of Control. For purposes of this Agreement, "Good Reason" shall be interpreted in a manner, and limited to the extent necessary, so that it shall not cause adverse tax

consequences for either party with respect to Section 409A ("Section 409A") of the Internal Revenue Code of 1986, as amended (the "Code") and any successor statute, regulation and guidance thereto.

3. Compensation.

(a) Base Salary. Commencing on the Start Date Company shall pay Executive a base salary (the "Base Salary") at the annual rate of Three Hundred Eighty Five Thousand Dollars ($385,000.00). The Base Salary shall be payable in substantially equal periodic installments in accordance with Company's payroll practices as in effect from time to time. Company shall deduct from each such installment all amounts required to be deducted or withheld under applicable law or under any employee benefit plan in which Executive participates. The Board or an appropriate committee thereof shall, on an annual basis, review the Base Salary, which may be adjusted upward (but not downward) at Company's discretion.

(b) Annual Performance Bonus. Commencing with fiscal year 2021, Executive shall be eligible to receive an annual cash bonus (the "Annual Performance Bonus"), with the target amount of such Annual Performance Bonus equal to forty percent (40%) of Executive's Base Salary in the year to which the Annual Performance Bonus relates; provided that the actual amount of the Annual Performance Bonus may be greater or less than such target amount. The amount of the Annual Performance Bonus shall be determined by the Board or an appropriate committee thereof in its sole discretion, and shall be paid to Executive no later than March 15th of the calendar year immediately following the calendar year in which it was earned. Except as provided in Section 4, Executive must be employed by Company on the last day of the applicable fiscal year to which the Annual Performance Bonus relates in order to be eligible for, and to be deemed as having earned, such Annual Performance Bonus. Company shall deduct from the Annual Performance Bonus all amounts required to be deducted or withheld under applicable law or under any employee benefit plan in which Executive participates.

(c) Equity. As a material inducement to the Executive joining the Company, on the Start Date, the Company shall award Executive an inducement stock option to purchase 75,000 shares of the Company's common stock, subject to approval by the Board or an authorized delegate thereof (the "Inducement Option Grant"). The Inducement Option Grant will be subject to the terms and conditions of the Company's 2019 Inducement Equity Incentive Plan, as amended, and the applicable option agreement between the Executive and the Company entered into pursuant thereto. The Inducement OptionGrant is intended as an inducement grant under Nasdaq Rule 5635(c)(4) and will not qualify as an incentive stock option. The exercise price of the stock options subject to the Inducement Option Grant shall be the closing price of the Company's common stock on the Nasdaq Stock Market on the Start Date. The Inducement Option Grant shall be evidenced in writing by, and subject to the terms of, a Company stock option agreement which shall specify vesting over four (4) years, 25% on the first anniversary of the Start Date with the balance to vest in equal monthly installments over the following 36 months, and exercise of vested options for up to ten (10) years except as otherwise provided in the stock option agreement. Commencing in fiscal year 2022, Executive shall be eligible to be considered for the grant of stock options and/or other equity-based awards commensurate with Executive's position and responsibilities. The amount, terms and conditions of any stock option or other equity-based award

shall be determined by the Board or an appropriate committee thereof in its discretion and set forth in the applicable equity plan and other documents governing the award.

(d) Paid Time Off. In addition to standard paid holidays, Executive may take up to twenty (20) days of paid time off ("PTO") per year, to be scheduled so as not to materially disrupt Company's operations, pursuant to the terms and conditions of Company policy and practices as applied to Company senior executives.

(e) Fringe Benefits. Executive shall be entitled to participate in all benefit/welfare plans and fringe benefits provided to Company senior executives. Executive understands that, except when prohibited by applicable law, Company's benefit plans and fringe benefits may be amended by Company from time to time in its sole discretion. The terms of any such benefits shall be governed by the applicable plan documents and Company policies in effect from time to time.

(f) Reimbursement of Expenses. Company shall reimburse Executive for all ordinary and reasonable out-of-pocket business expenses incurred by Executive in furtherance of Company's business in accordance with Company's policies with respect thereto as in effect from time to time. Executive must submit any request for reimbursement no later than ninety (90) days following the date that such business expense is incurred. All reimbursements provided under this Agreement shall be made or provided in accordance with the requirements of Section 409A including, where applicable, the requirement that (i) any reimbursement is for expenses incurred during Executive's lifetime (or during a shorter period of time specified in this Agreement); (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year; (iii) the reimbursement of an eligible expense shall be made no later than the last day of the calendar year following the year in which the expense is incurred; and (iv) the right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

(g) Indemnification. Executive shall be entitled to indemnification with respect to Executive's services provided hereunder pursuant to Delaware law, the terms and conditions of Company's certificate of incorporation and/or by-laws, and Company's standard indemnification agreement for directors and officers as executed by Company and Executive. Executive shall be entitled to coverage under the Company's Directors' and Officers' ("D&O") insurance policies that it may hold now or in the future to the same extent and in the same manner (i.e., subject to the same terms and conditions) that the Company's other executive officers are entitled to coverage under any of the Company's D&O insurance policies that it may have.

(h) Forfeiture/Clawback. All compensation shall be subject to any forfeiture or clawback policy established by Company generally for senior executives from time to time and any other such policy required by applicable law.

4. Payments Upon Termination.

(a) Definition of Accrued Obligations. For purposes of this Agreement, "Accrued Obligations" means: (i) the portion of Executive's Base Salary that has accrued prior to any termination of Executive's employment with Company and has not yet been paid; (ii) any

accrued but unused PTO pursuant to Company's standard policy and practices; and (iii) the amount of any expenses properly incurred by Executive on behalf of Company prior to any such termination and not yet reimbursed. Executive's entitlement to any other compensation or benefit under any plan of Company shall be governed by and determined in accordance with the terms of such plans, except as otherwise specified in this Agreement.

(b) Termination by Company for Cause. If Executive's employment hereunder is terminated by Company for Cause, then Company shall pay the Accrued Obligations to Executive promptly following the effective date of such termination and shall have no further obligations with respect to any benefit or compensation under this Agreement to Executive hereunder.

(c) Termination by Executive Without Good Reason. If Executive's employment hereunder is terminated by Executive without Good Reason, then Company shall pay the Accrued Obligations and any accrued and unpaid Annual Performance Bonus for the prior fiscal year to Executive promptly following the effective date of such termination and shall have no further obligations with respect to any benefit or compensation under this Agreement to Executive hereunder.

(d) Termination as a Result of Executive's Disability or Death. If Executive's employment hereunder terminates as a result of Executive's Disability or death, promptly after such termination Company shall pay to Executive (i) the Accrued Obligations; (ii) any accrued and unpaid Annual Performance Bonus for the prior fiscal year; and (iii) the Pro Rated Bonus (as defined below) and, shall have no further obligations with respect to any benefit or compensation under this Agreement to Executive hereunder. As used in this Section 4, "Pro Rated Bonus" shall mean an amount in cash equal to the target of Annual Performance Bonus for which Executive would have been eligible with respect to the year in which termination of Executive's employment occurs multiplied by a fraction, the numerator of which is the number of days during which Executive is employed by Company during the year of termination and the denominator of which is 365.

(e) Termination by Company Without Cause or by Executive For Good Reason. In the event that Executive's employment is terminated by action of Company other than for Cause, or Executive terminates Executive's employment for Good Reason, then, in addition to the Accrued Obligations and any accrued and unpaid Annual Performance Bonus for the prior fiscal year, Executive shall receive the following, subject to the terms and conditions described in Section 4(g) (including Executive's execution of the Release (as defined herein)):

(i) Severance Payments. Continuation of payments in an amount equal to Executive's then-current Base Salary for a nine (9) month period, less all customary and required taxes and employment-related deductions, in accordance with Company's normal payroll practices (provided such payments shall be made at least monthly), commencing on the first payroll date following the date on which the Release required by Section 4(g) becomes effective and non-revocable, but not after seventy (70) days following the effective date of termination from employment; provided, that if the 70th day falls in the calendar year following the year during which the termination or separation from service occurred, then the

payments shall commence in such subsequent calendar year; provided further that if such payments commence in such subsequent year, the first such payment shall be a lump sum in an amount equal to the payments that would have come due since Employee's separation from service.

(ii) Pro Rata Bonus. Payment of the Pro Rated Bonus, paid to Executive no later than March 15 of the calendar year next preceding the year of termination of employment, after deduction of all amounts required to be deducted or withheld under applicable law.

(iii) Benefits Payments. Upon completion of appropriate forms and subject to applicable terms and conditions under the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended ("COBRA"), Company shall continue to provide Executive medical insurance coverage to the same extent that such insurance continues to be provided to similarly situated executives at the time of Executive's termination with the cost of the regular premium for such benefits shared in the same relative proportion by Company and Executive as in effect on the last day of employment (the "COBRA Payment"), until the earlier to occur of: (i) twelve (12) months following Executive's termination date, or (ii) the date Executive becomes eligible for medical benefits with another employer. Notwithstanding the foregoing, if Executive's COBRA Payment would cause the applicable group health plan to be discriminatory and, therefore, result in adverse tax consequences to Executive, Company shall, in lieu of the COBRA Payment, provide Executive with an equivalent monthly cash payment, minus deduction of all amounts required to be deducted or withheld under applicable law, for any period of time Executive is eligible to receive the COBRA Payment. Executive shall bear full responsibility for applying for COBRA continuation coverage and Company shall have no obligation to provide Executive such coverage if Executive fails to elect COBRA benefits in a timely fashion.

Payment of the above described severance payments and benefits are expressly conditioned on Executive's execution without revocation of the Release and return of Company property under Section 6.

(f) Termination by Company Without Cause or by Executive For Good Reason Following a Change of Control. In the event that a Change of Control (as defined below) occurs and within a period of one (1) year following the Change of Control, or ninety (90) days preceding the earlier to occur of a Change of Control or the execution of a definitive agreement the consummation of which would result in a Change of Control, Executive's employment is terminated other than for Cause, or Executive terminates Executive's employment for Good Reason, then, in addition to the Accrued Obligations and any accrued and unpaid Annual Performance Bonus for the prior fiscal year, Executive shall receive the following, subject to the terms and conditions described in Section 4(g) (including Executive's execution of the Release):

(i) Lump Sum Severance Payment. Payment of a lump sum amount equal to twelve (12) months of Executive's then-current Base Salary plus the Pro Rated Bonus, less all customary and required taxes and employment-related

deductions, paid on the first payroll date following the date on which the Release required by Paragraph 4(g) becomes effective and non-revocable, but not after seventy (70) days following the effective date of termination from employment.

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

(iii) Benefit Payments. Upon completion of appropriate forms and subject to applicable terms and conditions under COBRA, Company shall continue to provide Executive medical insurance coverage to the same extent that such insurance continues to be provided to similarly situated executives at the time of Executive's termination with the cost of the regular premium for such benefits shared in the same relative proportion by Company and Executive as in effect on the last day of employment, until the earlier to occur of: (i) twelve (12) months following Executive's termination date, or (ii) the date Executive becomes eligible for medical benefits with another employer. Notwithstanding the foregoing, if Executive's COBRA Payment would cause the applicable group health plan to be discriminatory and, therefore, result in adverse tax consequences to Executive, Company shall, in lieu of the COBRA Payment, provide Executive with an equivalent monthly cash payment, minus deduction of all amounts required to be deducted or withheld under applicable law, for any period of time Executive is eligible to receive the COBRA Payment. Executive shall bear full responsibility for applying for COBRA continuation coverage and Company shall have no obligation to provide Executive such coverage if Executive fails to elect COBRA benefits in a timely fashion.

Payment of the above described severance payments and benefits are expressly conditioned on Executive's execution without revocation of the Release and return of Company property under Section 6. In the event that Executive is eligible for the severance payments and benefits under this Section 4(f), Executive shall not be eligible for any of the severance payments and benefits as provided in Section 4(e).

As used herein, a "Change of Control" shall mean the occurrence of any of the following events: (i) Ownership. Any "Person" (as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended) becomes the "Beneficial Owner" (as defined in Rule 13d-3 under said Act), directly or indirectly, of securities of Company representing fifty percent (50%) or more of the total voting power represented by Company's then outstanding voting securities (excluding for this purpose any such voting securities held by Company, or any affiliate, parent or subsidiary of Company, or by any employee benefit plan of Company) pursuant

to a transaction or a series of related transactions; or (ii) Merger/Sale of Assets. (A) A merger or consolidation of Company whether or not approved by the Board, other than a merger or consolidation which would result in the voting securities of Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or the parent of such corporation) at least fifty percent (50%) of the total voting power represented by the voting securities of Company or such surviving entity or parent of such corporation, as the case may be, outstanding immediately after such merger or consolidation; (B) or Company's stockholders approve an agreement for the sale or disposition by Company of all or substantially all of Company's assets; or (iii) Change in Board Composition. A change in the composition of the Board, as a result of which fewer than a majority of the directors are Incumbent Directors. "Incumbent Directors" shall mean directors who either (A) are directors of Company as of the date of this Agreement, or (B) are elected, or nominated for election, to the Board with the affirmative votes of at least a majority of the Incumbent Directors, or by a committee of the Board made up of at least a majority of the Incumbent Directors, at the time of such election or nomination (but shall not include an individual whose election or nomination is in connection with an actual or threatened proxy contest relating to the election of directors).

(g) Execution of Release of Claims. Company shall not be obligated to pay Executive any of the severance payments or benefits described in this Section 4 unless and until Executive has executed (without revocation) a release of claims as described below (the "Release"). The Release shall contain reasonable and customary provisions including a general release of claims against Company and its affiliated entities and each of their officers, directors and employees as well as mutual non-disparagement, non-competition, non-solicitation, confidentiality, cooperation and the like. The Release must be provided to Executive not later than fifteen (15) days following the effective date of termination of Executive's employment by Company and executed by Executive and returned to Company within sixty (60) days after such effective date. If Executive fails or refuses to return the Release within such 60-day period, Executive's severance payments and benefits to be paid hereunder shall be forfeited.

(h) No Other Payments or Benefits Owing. Except as expressly set forth herein, the payments and benefits set forth in this Section 4: (a) shall be the sole amounts owing to Executive upon termination of Executive's employment for the reasons set forth above, and Executive shall not be eligible for any other payments or other forms of compensation or benefits; (b) shall be the sole remedy, if any, available to Executive in the event that Executive brings any claim against Company relating to the termination of Executive's employment under this Agreement; and (c) shall not be subject to set-off by Company or any obligation on the part of Executive to mitigate or to offset compensation earned by Executive in other pursuits after termination of employment, other than as specified herein with respect to medical benefits provided by another employer.

5. Prohibited Competition and Solicitation. Executive expressly acknowledges that: (a) there are competitive and proprietary aspects of the business of Company; (b) during the course of Executive's employment, Company shall furnish, disclose or make available to Executive confidential and proprietary information and may provide Executive with unique and specialized training; (c) such Confidential Information and training have been developed and shall

be developed by Company through the expenditure of substantial time, effort and money, and could be used by Executive to compete with Company; and (d) in the course of Executive's employment, Executive shall be introduced to customers and others with important relationships to Company, and any and all "goodwill" created through such introductions belongs exclusively to Company, including, but not limited to, any goodwill created as a result of direct or indirect contacts or relationships between Executive and any customers of Company. In light of the foregoing acknowledgements, and as a condition of employment hereunder, Executive hereby approves the Restrictive Covenant Agreement entered into on the date hereof as a binding obligation of the Executive, enforceable in accordance with its terms.

6. Property and Records. Upon the termination of Executive's employment hereunder for any reason or for no reason, or if Company otherwise requests, Executive shall: (a) return to Company all tangible business information and copies thereof (regardless how such Confidential Information or copies are maintained), and (b) deliver to Company any property of Company which may be in Executive's possession, including, but not limited to, Blackberry-type devices, smart phones, laptops, cell phones (the foregoing, "electronic devices"), products, materials, memoranda, notes, records, reports or other documents or photocopies of the same. Executive may retain copies of any exclusively personal data contained in or on Company-owned electronic devices returned to Company pursuant to the foregoing. The foregoing notwithstanding, Executive understands and agrees that Company property belongs exclusively to Company, it should be used for Company business, and Executive has no reasonable expectation of privacy on any Company property or with respect to any information stored thereon.

7. Cooperation. During and after Executive's employment, Executive shall fully cooperate with Company to the extent reasonable in the defense or prosecution of any claims or actions now in existence or which may be brought in the future against or on behalf of Company (other than claims directly or indirectly against Executive) which relate to events or occurrences that transpired while Executive was employed by Company. Executive's cooperation in connection with such claims or actions shall include, but not be limited to, being available to meet with counsel to prepare for discovery or trial and to act as a witness on behalf of Company at mutually convenient times. During and after Executive's employment, Executive also shall fully cooperate with Company to the extent reasonable in connection with any investigation or review of any federal, state or local regulatory authority as any such investigation or review relates to events or occurrences that transpired while Executive was employed by Company. Company shall reimburse Executive for any reasonable out-of-pocket expenses incurred in connection with the Executive's performance of obligations pursuant to this section. In addition, Company shall compensate Executive on an hourly basis, based on a rate commensurate with Executive's Base Salary in effect prior to termination, for time Executive spends in excess of 10 hours in any calendar quarter providing services to the Corporation after termination.

8. Code Sections 409A and 280G.

(a) In the event that the payments or benefits set forth in Section 4 of this Agreement constitute "non-qualified deferred compensation" subject to Section 409A, then the following conditions apply to such payments or benefits:

(i) Any termination of Executive's employment triggering payment of benefits under Section 4 must constitute a "separation from service" under Section 409A(a)(2)(A)(i) of the Code and Treas. Reg. §1.409A-1(h) before distribution of such benefits can commence. To the extent that the termination of Executive's employment does not constitute a separation of service under Section 409A(a)(2)(A)(i) of the Code and Treas. Reg. §1.409A-1(h) (as the result of further services that are reasonably anticipated to be provided by Executive to Company at the time Executive's employment terminates), any such payments under Section 4 that constitute deferred compensation under Section 409A shall be delayed until after the date of a subsequent event constituting a separation of service under Section 409A(a)(2)(A)(i) of the Code and Treas. Reg. §1.409A-1(h). For purposes of clarification, this Section 8(a) shall not cause any forfeiture of benefits on Executive's part, but shall only act as a delay until such time as a "separation from service" occurs.

(ii) Notwithstanding any other provision with respect to the timing of payments under Section 4 if, at the time of Executive's termination, Executive is deemed to be a "specified employee" of Company (within the meaning of Section 409A(a)(2)(B)(i) of the Code), then limited only to the extent necessary to comply with the requirements of Section 409A, any payments to which Executive may become entitled under Section 4 which are subject to Section 409A (and not otherwise exempt from its application) shall be withheld until the first (1st) business day of the seventh (7th) month following the termination of Executive's employment, at which time Executive shall be paid an aggregate amount equal to the accumulated, but unpaid, payments otherwise due to Executive under the terms of Section 4.

(b) It is intended that each installment of the payments and benefits provided under Section 4 of this Agreement shall be treated as a separate "payment" for purposes of Section 409A. Neither Company nor Executive shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

(c) Notwithstanding any other provision of this Agreement to the contrary, this Agreement shall be interpreted and at all times administered in a manner that avoids the inclusion of compensation in income under Section 409A, or the payment of increased taxes, excise taxes or other penalties under Section 409A. The parties intend this Agreement to be in compliance with Section 409A. Executive acknowledges and agrees that Company does not guarantee the tax treatment or tax consequences associated with any payment or benefit arising under this Agreement, including but not limited to consequences related to Section 409A.

(d) If any payment or benefit Executive would receive under this Agreement, when combined with any other payment or benefit Executive receives pursuant to a Change of Control (for purposes of this section, a "Payment") would: (i) constitute a "parachute payment" within the meaning of Section 280G the Code; and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either: (A) the full amount of such Payment; or (B) such lesser amount (with cash payments being

reduced before stock option compensation) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employments taxes, income taxes, and the Excise Tax, results in Executive's receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax. Notwithstanding the foregoing, if, prior to the closing of an initial public offering, any Payment can be exempt from the definition of "parachute payment" and the Excise Tax pursuant to the shareholder approval requirements described in Treas. Regs. § 1.280G-1, Q&A 6, the Company will, at the Executive's election (and subject to the Executive signing an appropriate waiver) seek shareholder approval to exempt such Payment from the definition of "parachute payment" and the Excise Tax.

9. General.

(a) Notices. Except as otherwise specifically provided herein, any notice required or permitted by this Agreement shall be in writing and shall be delivered as follows with notice deemed given as indicated: (i) by personal delivery when delivered personally; (ii) by overnight courier upon written verification of receipt; (iii) by telecopy or facsimile transmission upon acknowledgment of receipt of electronic transmission; or (iv) by certified or registered mail, return receipt requested, upon verification of receipt.

Notices to Executive shall be sent to the last known address in Company's records or such other address as Executive may specify in writing.

Notices to Company shall be sent to:

Spero Therapeutics, Inc.
675 Massachusetts Ave., 14th Floor
Cambridge, MA 02139
Attn: CEO

(b) Modifications and Amendments. The terms and provisions of this Agreement may be modified or amended only by written agreement executed by the parties hereto.

(c) Waivers and Consents. The terms and provisions of this Agreement may be waived, or consent for the departure therefrom granted, only by a written document executed by the party entitled to the benefits of such terms or provisions. No such waiver or consent shall be deemed to be or shall constitute a waiver or consent with respect to any other terms or provisions of this Agreement, whether or not similar. Each such waiver or consent shall be effective only in the specific instance and for the purpose for which it was given and shall not constitute a continuing waiver or consent.

(d) Assignment. Company may assign its rights and obligations hereunder to any person or entity that succeeds to all or substantially all of Company's business or that aspect of Company's business in which Executive is principally involved. Executive may not assign Executive's rights and obligations under this Agreement without the prior written consent of Company.

(e) Governing Law/Dispute Resolution. This Agreement and the rights and obligations of the parties hereunder shall be construed in accordance with and governed by the law of the Commonwealth of Massachusetts without giving effect to the conflict of law principles thereof. Any legal action or proceeding with respect to this Agreement shall be brought in the courts of the Commonwealth of Massachusetts or of the United States of America for the District of Massachusetts. By execution and delivery of this Agreement, each of the parties hereto accepts for itself and in respect of its property, generally and unconditionally, the non-exclusive jurisdiction of the aforesaid courts.

(f) Jury Waiver. ANY, ACTION, DEMAND, CLAIM, OR COUNTERCLAIM ARISING UNDER OR RELATING TO THIS AGREEMENT SHALL BE RESOLVED BY A JUDGE ALONE, AND EACH OF COMPANY AND EXECUTIVE WAIVES ANY RIGHT TO A JURY TRIAL THEREOF.

(g) Headings and Captions. The headings and captions of the various subdivisions of this Agreement are for convenience of reference only and shall in no way modify or affect the meaning or construction of any of the terms or provisions hereof.

(h) Entire Agreement. This Agreement, together with the other agreements specifically referenced herein, embodies the entire agreement and understanding between the parties hereto with respect to the subject matter hereof and supersedes all prior oral or written agreements and understandings relating to the subject matter hereof. No statement, representation, warranty, covenant or agreement of any kind not expressly set forth in this Agreement shall affect, or be used to interpret, change or restrict, the express terms and provisions of this Agreement.

(i) Counterparts. This Agreement may be executed in two or more counterparts, and by different parties hereto on separate counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. For all purposes a signature by fax shall be treated as an original.

[Signature Page to Follow]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first written above.

TAMARA JOSEPH

/s/ Tamara Joseph
Signature

SPERO THERAPEUTICS, INC.

By: /s/ Ankit Mahadevia
Name: Ankit Mahadevia
Title: CEO

Exhibit 10.25

AMENDED AND RESTATED LICENSE AGREEMENT

This AMENDED AND RESTATED LICENSE AGREEMENT (this "**Agreement**") , effective as of January 15, 2021 (the "**Amendment Effective Date**"), is entered into by and among **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; **Spero Therapeutics, Inc.**, a Delaware corporation ("**Spero**") having its principal place of business at 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts, 02139; and, solely for purposes of Section 3.3(e) (with respect to the SPR741 Option), **Spero Potentiator, Inc.**, a Delaware corporation ("**Potentiator**") having its principal place of business at 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts, 02139. Everest, Spero and Potentiator are referred to individually as a "**Party**" and collectively as the "**Parties**."

RECITALS

WHEREAS, **New Pharma License Holdings Limited** ("**NPLH**", a company organized under the laws of Malta having registration number C 75891 and its principal place of business at 675 Massachusetts Avenue, 14th Floor, Cambridge, Massachusetts, 02139) was the previous owner of 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;

WHEREAS, NPLH, Everest and Potentiator entered into a license agreement (the "**Original License**") dated January 1, 2019 (the "**Effective Date**"), under which (i) NPLH granted a license to Everest under certain intellectual property rights of NPLH at that time to develop and commercialize SPR206 in certain territories; and (ii) Potentiator granted an exclusive option to Everest to negotiate for an exclusive license to use certain intellectual property rights of Potentiator to develop and commercialize SPR741 in certain territories (the "**SPR741 Option**");

WHEREAS, pursuant to the notice and consent to assignment of licensed technology issued to Everest by NPLH and Spero dated June 18, 2020, NPLH assigned to Spero all of the business and assets of NPLH related to the Original License, including without limitation, the Licensed Technology (as defined under the Original License), and Spero agreed to be responsible to Everest for the performance of all the obligations of NPLH under the Original License;

WHEREAS, Spero has now agreed to assign to Everest, and Everest has agreed to accept, all the Licensed Patents under the Original License (referred to as "**Assigned Patents**" under this

Agreement, as more particularly defined under ARTICLE 1); provided that, upon the occurrence of certain specified events, Spero shall have an exclusive option to acquire back the Assigned Patents, in accordance with the terms of this Agreement;

WHEREAS, Everest has now determined not to exercise the SPR741 Option under the Original License, and Everest and Potentiator have agreed that all the provisions of the Original License associated with the SPR741 Option shall cease to have effect; and

WHEREAS, Spero and Everest now desire to amend and restate in its entirety the Original License to reflect the abovementioned consensus, together with other agreed commercial terms, such amendment effective as of the Amendment Effective Date.

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 "**Assigned Patents**" means all Patents Controlled by Spero in the Territory as of the Amendment 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 Spero Sole Invention Patents in the Territory. For clarity, "Assigned Patents" includes 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 Controlled by Spero (including, for the avoidance of doubt, the national applications for [***] filed in any jurisdiction in the Territory upon Everest's request). The Assigned Patents existing as of the Amendment Effective Date are listed on Exhibit A.

1.5 "**Assignment**" has the meaning set forth in Section 2.1 (Assignment).

1.6 "**Auditor**" has the meaning set forth in Section 9.10 (Audit Dispute).

1.7 "**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.

1.8 "**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.

1.9 "**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.

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

1.11 "**Challenge"** means to contest or assist, directly or indirectly, in the contesting of the validity or enforceability of any of the Assigned 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 Assigned 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 Assigned Patents; (c) filing a request under 35 U.S.C. § 302 for re-examination of any of the Assigned Patents; (d) filing, or

joining in, a petition under 35 U.S.C. § 311 to institute inter partes review of any Assigned 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 Assigned Patents or any portion thereof; (f) provoking or becoming a party to an interference with an application for any of the Assigned 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 Assigned Patents in any country; or (h) any foreign equivalents of subsection (a) through (g) applicable in the Territory.

1.12 "**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.

1.13 "**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.

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

1.15 "**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.

1.16 **"Commercial Supply Agreement**" has the meaning set forth in Section 7.1(b) (Commercial Supply Agreement).

1.17 "**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.

1.18 "**Commercialization Plan"** has the meaning set forth in Section 8.2 (Commercialization Plan).

1.19 "**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.

1.20 "**Completion**" means the completion of the manufacturing technology transfer from Spero to Everest contemplated under Section 7.2, including, without limitation, (i) the transfer or having made available to Everest by or on behalf of Spero of all the Licensed Manufacturing Know-How possessed and Controlled by Spero; and (ii) the completion of all necessary introductions and required permissions relating to existing Spero CMOs.

1.21 "**Compound**" means SPR206.

1.22 "**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.

1.23 "**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.

1.24 "**Controlling Party**" has the meaning set forth in Section 10.6 (Invalidity or Unenforceability Defenses or Actions)

1.25 **"Corporate Names"** has the meaning set forth in Section 1.124 (Spero Trademarks).

1.26 "**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 Spero or its Affiliates.

1.27 **"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.

1.28 "**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.

1.29 "**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.

1.30 "**Development Plan"** has the meaning set forth in Section 5.2 (Development Plan).

1.31 "**Diligence Meeting**" has the meaning set forth in Section 5.3(b) (Specific Diligence Events).

1.32 "**Diligence Meeting Date**" has the meaning set forth in Section 5.3(b) (Specific Diligence Events).

1.33 "**Diligence Milestone**" has the meaning set forth in Section 5.3(b) (Specific Diligence Events).

1.34 "**Diligence Target Dates**" has the meaning set forth in Section 5.3(b) (Specific Diligence Events).

1.35 "**Disclosing Party"** has the meaning set forth in Section 11.1(a) (Duty of Confidence - subsection (a)).

1.36 "**Dispute"** has the meaning set forth in Section 15.10(a) (Dispute Resolution - subsection (a)).

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

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

1.39 "**Everest Development Data**" means any (a) pharmacology, toxicology and other biological 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 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.

1.40 "**Everest Know-How**" means all Know-How that Everest Controls as of the Amendment 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.

1.41 "**Everest Indemnitees**" has the meaning set forth in Section 14.1 (Indemnification by Spero).

1.42 "**Everest Patents**" means all Patents that Everest Controls as of the Amendment 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 the Assigned Patents, any Everest Sole Invention Patents, any Joint Patents in the Territory, and Everest's interest in any Joint Patents outside the Territory.

1.43 "**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.

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

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

1.46 "**Excluded Claim"** has the meaning set forth in Section 15.10(g) (Dispute Resolution - subsection (g)).

1.47 **"Executive Officers"** has the meaning set forth in Section 4.3(b) (JDC Decision Making - subsection (a)).

1.48 "**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.

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

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

1.51 "**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).

1.52 "**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.

1.53 "**First Diligence Notice**" has the meaning set forth in Section 5.3(b) (Specific Diligence Events).

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

1.55 "**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.

1.56 "**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).

1.57 "**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.

1.58 **"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.

1.59 "**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).

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

1.61 "**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.

1.62 "**Indemnification Claim Notice**" has the meaning set forth in Section 14.3(a) (Notice of Claim).

1.63 "**Indemnified Party**" has the meaning set forth in Section 14.3(a) (Notice of Claim).

1.64 "**Indemnifying Party**" has the meaning set forth in Section 14.3(a) (Notice of Claim).

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

1.66 "**Indirect Costs**" means, with respect to a multi-regional clinical trial, all Third Party costs and expenses incurred by Spero 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.

1.67 **"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) Spero'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) Spero's Manufacturing, selling or offering for sale of the Compound or a Licensed Product.

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

1.69 "**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.

1.70 "**Initial Supply Agreement**" has the meaning set forth in Section 7.1 (Supply Agreement).

1.71 "**Initial Term**" has the meaning set forth in Section 12.1 (Term).

1.72 "**In-License Agreement**" has the meaning set forth in Section 3.4(b) (In-License Agreements).

1.73 "**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 Spero Development Data or Everest Development Data.

1.74 "**Joint Development Committee**" or "**JDC**" has the meaning set forth in Section 4.1 (Joint Development Committee).

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

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

1.77 "**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.

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

1.79 "**Licensed Know-How**" means all Know-How that Spero Controls as of the Amendment 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 Spero Sole Inventions in the Territory, Spero Development Data and Spero Regulatory Documentation (with respect to Compound or a Licensed Product).

1.80 "**Licensed Manufacturing Know-How**" has the meaning set forth in Section 7.2 (Manufacturing Technology Transfer).

1.81 "**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 Licensed Product for one or more additional Indications shall not constitute a new and separate Licensed Product.

1.82 "**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) 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.

1.83 "**Licensed Technology**" means the Licensed Know-How and, if applicable in accordance with the provisions of Section 3.4(b) (In-License Agreements), Infringed IP that Third Parties have licensed to Spero under the relevant In-License Agreements.

1.84 "**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.

1.85 "**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.

1.86 "**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.

1.87 "**Manufacturing Transfer Period**" has the meaning set forth in Section 7.2 (Manufacturing Technology Transfer).

1.88 "**Milestone Event**" has the meaning set forth in Section 9.2 - (8.2 Development and Regulatory Milestone Payments – clause (a)).

1.89 "**Milestone Payment**" has the meaning set forth in Section 9.2 - (8.2 Development and Regulatory Milestone Payments – clause (a)).

1.90 "**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.

1.91 "**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).

1.92 "**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.

1.93 "**Original License**" has the meaning set forth in the Recitals.

1.94 "**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.

1.95 "**Payment"** has the meaning set forth in Section 9.8(b).

1.96 "**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.

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

1.98 "**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.

1.99 "**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.

1.100 "**Polymyxin Class Compound**" has the meaning set forth in Section 3.8 (Non-Compete).

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

1.102 "**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.

1.103 "**Product Infringement**" has the meaning set forth in Section 10.4(a) (Notice).

1.104 "**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 or its Affiliates or its (sub)licensees (or Sublicensees)).

1.105 "**Receiving Party"** has the meaning set forth in Section 11.1(a) (Duty of Confidence - subsection (a)).

1.106 "**Reimbursement Rate**" means, with respect the costs to Spero 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.

1.107 "**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.

1.108 "**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.

1.109 **"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.

1.110 "**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.

1.111 "**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.

1.112 "**Representative**" has the meaning set forth in Section 11.1(c) (Duty of Confidence - Subsection (c)).

1.113 "**Respective Territory**" means, in the case of Everest, the Territory, and in the case of Spero, all countries of the world outside the Territory.

1.114 "**Retained Rights**" means:

(i) with respect to the Compound and Licensed Products, the rights of Spero, 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; and

(ii) with respect to any compounds other than the Compound and any products other than the Licensed Products, the rights of Spero, its Affiliates and its and their licensors, (sub)licensees and contractors to make, use, import, export, research, develop, manufacture, hold or keep, or have made, used, imported, exported, researched, developed, manufactured, held or kept, such other compounds and products within the Territory solely for marketing, offering for sale or commercialization outside the Territory.

1.115 "**Royalty Term**" has the meaning set forth in Section 9.4(b) (Royalty Term).

1.116 "**SEC**" has the meaning set forth in Section 11.5 (Publicity/Use of Names - subsection (a)).

1.117 "**Senior Officer**" means, with respect to Spero, its Chief Executive Officer, and with respect to Everest, its Chief Executive Officer.

1.118 "[***]" has the meaning set forth in Section 15.10(b) (Dispute Resolution).

1.119 "**Spero CMO**" has the meaning set forth in Section 7.2 (Manufacturing Technology Transfer)

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

1.121 "**Spero Indemnitees**" has the meaning set forth in Section 14.2 (Indemnification by Everest).

1.122 "**Spero Sole Inventions**" means any Inventions that are conceived and reduced to practice solely by employees of, or consultants or service providers to, Spero, 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, which Inventions relate solely and exclusively to the Compound and Licensed Products or the method of use or manufacture thereof, and not to any other compound, structure or composition of matter or the method of use or manufacture thereof.

1.123 "**Spero Sole Invention Patents**" means any Patents in the Territory that contain one or more claims that cover Spero Sole Inventions.

1.124 "**Spero Trademarks**" means any corporate name or corporate logo of Spero or its Affiliates, and any Trademark that consists of or includes any corporate name or corporate logo of Spero or its Affiliates ("**Corporate Names**"), including the Spero Trademarks, names and logos identified on Exhibit B hereto and such other Trademarks, names and logos as Spero may designate in a writing sent to Everest from time to time during the Term.

1.125 "**SPR206**" means the compound known as SPR206 and having the chemical structure shown in Exhibit C and [***].

1.126 "**SPR741**" means the compound known as SPR741 and having the chemical structure shown in Exhibit D and [***].

1.127 "**SPR741 Option**" has the meaning set forth in the Recitals.

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 3.1(Licenses to Everest).

1.129 "**Subcontractor**" has the meaning set forth in Section 3.9 (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 12.1 (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 12.1 (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 10.5 (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 9.8(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
ASSIGNMENT

2.1 **Assignment.**

(a) Spero hereby assigns, transfers and sets over to Everest all of its right, title and interest in and to any and all Assigned Patents (the "**Assignment**"), including, without limitation, all statutory and common law rights attaching to the Assigned Patents (including the right to file application, prosecution and maintenance of any Assigned Patents), now or hereafter in effect, for Everest's own use and enjoyment, and for the use and enjoyment of Everest's successors, assigns or other legal representatives, as fully and entirely as the same would have been held and enjoyed by Spero if this Assignment has not been made, together with all income, royalties, damages or payments due or payable as of the Amendment Effective Date or thereafter (excluding all income, royalties, damages or payments due or payable to Spero pursuant to this Agreement), including, without limitation and except as otherwise set forth in this Agreement, all claims for damages by reason of past, present or future infringement or other unauthorized use of the Assigned Patents, with the right to sue for, and collect the same for its own use and enjoyment, and for the use and enjoyment of its successors, assigns or other legal representatives.

(b) Spero and Everest shall, at Everest's expense, cooperate to prepare and file deeds of assignments or such other instruments of assignment in the patent office or any equivalent government agency in the relevant jurisdictions in the Territory as are necessary to record Everest as the owner of the Assigned Patents, and Spero agrees to provide (at Everest's expense) any assistance reasonably required by Everest to record and perfect such transfer of ownership of the Assigned Patents.

(c) Without affecting any other provision of this Agreement, Spero unconditionally and irrevocably covenants, without limitation in time, that it shall not, and that it shall ensure that its licensees do not, assert or raise against Everest or any of its licensees or assignees, any claim or action in relation to any use of the Assigned Patents after the Amendment Effective Date.

(d) Each Party shall perform (or procure the performance of) all further acts and things and execute and deliver (or procure the execution and delivery of) such further documents, as may be required by Applicable Law or as may be necessary or reasonably required by Everest to implement and give effect to the Assignment.

(e) At any time during the Term if (i) Everest desires to discontinue the development and commercialization of the Compound and the Licensed Products, or (ii) this Agreement is terminated (A) by Everest pursuant to Section 12.2(a), or (B) by Spero pursuant to Section 12.2(b), 12.2(b) or 12.2(d), then Everest shall (1) grant Spero the license as applicable on the terms of Section 12.3(c) (Consequences of Termination), and (2) promptly (but in no event later than [***] days before an action is due where inaction would result in abandonment of and Assigned Patent) notify Spero in writing and Spero shall have an exclusive option, exercisable within [***] days after the receipt of such notice, to notify Everest in writing of its intent to acquire back the Assigned Patents. Upon receiving Spero's notice of its intent to so acquire back the Assigned Patents Everest shall assign any of the affected Assigned Patents back to Spero on the same material terms and conditions as those of the Assignment under Section 2.1 (except this Section 2.1(e) and Section 2.1(e)).

(f) At any time during the Term if Everest desires to abandon any, but not all, of the Assigned Patents (including an Assigned Patent added after the Amendment Effective Date) or any Joint Patent, then Everest shall notify Spero in writing promptly (but in no event later than [***] days before an action is due where inaction would result in abandonment of such Assigned Patent(s)) or such Joint Patent and Spero shall have an exclusive option, exercisable within [***] days after the receipt of such notice, to notify Everest in writing if it intends to acquire back the affected Assigned Patents and/or to acquire Everest's interest in such Joint Patent. Upon receiving Spero's notice, Everest shall assign any of the affected Assigned Patents and/or its rights in such Joint Patent to Spero on the same material terms and conditions as those of the Assignment under this Section 2.1 (except Section 2.1(e) and this Section 2.1(e)).

ARTICLE 3
LICENSES

3.1 License to Everest.

(a) Subject to the terms and conditions of this Agreement, Spero hereby grants to Everest an exclusive (even as to Spero), royalty-bearing license under the Licensed Technology solely to Exploit Licensed Products in the Licensed Field in the Territory, with the right to grant sublicenses in accordance with Section 3.3 (Sublicense Rights).

(b) The United States federal government retains rights in certain of the Assigned 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.

3.2 License to Spero. Subject to the terms and conditions of this Agreement, Everest hereby grants to Spero an exclusive (even as to Everest), royalty-free license under the Everest Technology (excluding Assigned Patents, Everest Sole Invention Patents in the Territory, and Joint Patents in the Territory) solely to Exploit Licensed Products in the Licensed Field outside the Territory, with the right to grant sublicenses in accordance with Section 3.3 (Sublicense Rights).

3.3 Sublicense Rights.

(a) **Affiliates.** Subject to the terms of this Section 3.3 (Sublicense Rights), Everest may grant a sublicense of the license granted in Section 3.1 (License to Everest) through multiple tiers to Affiliates of Everest without prior notice to or the prior consent of Spero; provided that (i) 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 (ii) Everest shall be responsible for all actions, activities and obligations to Spero of such Affiliate. Subject to the terms of this Section 3.3 (Sublicense Rights), Spero may grant a sublicense of the license granted in Section 3.2 (License to Spero) through multiple tiers to Affiliates of Spero without prior notice to or the prior consent of Everest; provided that (i) Spero 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 (ii) Spero shall be responsible for all actions, activities and obligations to Everest of such Affiliate.

(b) **Third Parties.** Upon the prior written consent of Spero, such consent not to be unreasonably withheld, conditioned, or delayed, Everest may grant a sublicense of the rights granted under the license in Section 3.1 (License to Everest) through multiple tiers to any Third Party; provided that (i) 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; (ii) Spero 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 (iii) Everest shall be responsible to Spero for a breach of this Agreement due to the breach by such Third Party of such sublicense agreement. Everest hereby waives any

requirement that Spero 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, Spero may grant a sublicense of the rights granted under the license in Section 3.2 (License to Spero) through multiple tiers to any Third Party; provided that (i) 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; (ii) Everest shall be provided by Spero with a copy of such sublicense agreement within [***] days of execution, which copy may redact any financial or other priority terms; and (iii) Spero shall be responsible to Everest for a breach of this Agreement due to the breach by such Third Party of such sublicense agreement. Spero 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 Spero.

(c) A copy of each sublicense agreement with any Third Party shall, without redaction, be made available to (i) pursuant to Section 9.9 (Financial Records and Audit), any independent certified public accountant for the purpose of verifying for Spero 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 Spero pursuant to this Agreement and (ii) pursuant to Section 9.10 (Audit Dispute), any Auditor resolving a financial disagreement between the Parties.

(d) For clarity, the rights of the Parties under Section 6.3 (Rights of Reference) are separate and distinct from the rights to sublicense pursuant to this Section 3.3 (Sublicense Rights).

(e) Under the Original License, Potentiator granted to Everest an exclusive SPR741 Option, exercisable by written notice from Everest to Potentiator 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. Everest and Potentiator acknowledge that Everest has now determined not to exercise the SPR741 Option under the Original License, and Everest and Potentiator agree that all the terms of the Original License associated with the SPR741 Option shall cease to have effect as of the Amendment Effective Date and shall be removed from this Agreement.

3.4 Spero's Retained Rights; Limitations of License Grants.

(a) **Retained Rights of Spero**. Notwithstanding anything to the contrary in this Agreement and without limitation of any rights granted or reserved to Spero pursuant to any other term or condition of this Agreement, Spero 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 Assigned Patents, the Licensed Know-How, Spero Development Data, Spero's interests in and to Joint Patents and Joint Know-How, Regulatory Documentation of Spero and the Corporate Names of Spero and its Affiliates, in each case, for purposes of performing or exercising the Retained Rights.

(b) **In-License Agreements**

A. If Spero or any of its Affiliates intends to negotiate with a Third Party at arms' length to obtain a license to Infringed IP (an "**In-License Agreement**"), then Spero shall promptly notify Everest and identify the relevant Third Party's Infringed IP, with a copy to the JDC, and obtain Everest's prior written consent before entering into any In-License Agreement. The applicable Third Party's Infringed IP shall be included in the license granted to Everest under Section 3.1 (License to Everest) and considered Licensed Technology, respectively, only if Spero discloses the substantive terms of the In-License Agreement to Everest, which Spero 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 3.1 (License to Everest) nor considered to be Licensed Technology.

B. Subject to Section 3.4(b)F (In-License Agreements) below, 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 Spero 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 Spero under Section 3.2 (License to Spero) and considered Everest Patents and Everest Know-How, respectively, only if Everest discloses the substantive terms of such Third Party license to Spero, which Everest hereby agrees to do, and Spero 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 Spero 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, Spero 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 Spero under Section 3.2 (License to Spero) nor considered to be Everest Patents and Everest Know-How. In the event that Spero does agree to accept such Third Party license, the provisions of clauses (3), (4) and (5) of this Section 3.4(b) (In-License Agreements) shall apply, *mutatis, mutandis*, to any such Third Party license.

C. Subject to this Section 3.4(b) (In-License Agreements), the licenses granted by Spero in Section 3.1 (License to Everest) includes sublicenses solely under the applicable license rights granted to Spero 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.

D. The Parties shall cooperate with each other in good faith to support each other in complying with Spero'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 Spero 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.

E. On an In-License Agreement-by-In-License Agreement basis, from and after the date on which Everest agrees in writing pursuant to Section 3.4(b)A to accept the Patents and Know-How covered by such In-License Agreement as Licensed Technology under this Agreement, Spero 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.

F. If Everest either intends or has the opportunity to negotiate a license to, in each case in any jurisdiction located outside 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 could reasonably be infringed by Spero's Manufacturing, selling or offering for sale of the Compound or a Licensed Product; and in the case of (c), which Know-How is reasonably necessary to Spero's Manufacturing, selling or offering for sale of the Compound or a Licensed Product (collectively, "**Non-Territory Infringed IP**"), then Everest shall promptly notify Spero and identify the relevant Third Party's Non-Territory Infringed IP, with a copy to the JDC, and obtain Spero's prior written consent before entering into a license to any such Third Party's Non-Territory Infringed IP (a "**Non-Territory License**"). The applicable Third Party's Non-Territory Infringed IP shall be included in the license granted by Everest to Spero under Section 3.2 (License to Spero) and considered Everest Patents and Everest Know-How, respectively, only if Everest discloses the substantive terms of such Non-Territory License to Spero, which Everest hereby agrees to do, and Spero agrees in writing to (A) comply with all the relevant obligations of such Non-Territory 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 Spero reasonably determines that such Third Party's Non-Territory 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, Spero has the right not to pay any costs associated with such Non-Territory License, in which case such Third Party's Non-Territory Infringed IP shall not be included in the license granted to Spero under Section 3.2 (License to Spero) nor considered to be Everest Patents and Everest Know-How. In the event that Spero does agree to accept such Non-Territory License, the provisions of clauses (3), (4) and (5) of this Section 3.4(b) (In-License Agreements) shall apply, *mutatis, mutandis*, to any such Non-Territory License

3.5 Initial Transfer of Know-How. Upon the written request of Everest, Spero shall commence disclosing and making available to Everest the Licensed Know-How (including the Spero 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 Spero, each of which shall cooperate with each other in good faith to enable a smooth transfer of the Licensed Know-How from Spero to Everest. Upon Everest's reasonable request during such transfer, Spero 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. Spero shall be responsible for only the costs associated with the first [***] FTE hours of activities by such employees and advisors under this Section 3.5 and the activities described in Section 7.2 (whether under this Agreement or the Original Agreement) and (ii) Everest shall be responsible for any costs and expenses of any such activities under this Section 3.5 and Section 7.2 once such [***]-FTE threshold is used, and shall pay or reimburse Spero at the Reimbursement Rate following a written invoice in reasonable detail.

3.6 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.

3.7 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 Spero.

3.8 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 3.8 with regard to a particular Polymyxin Class Compound and/or a particular transaction, Spero will in good faith give due consideration to such request. Notwithstanding the foregoing, if 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 3.8.

3.9 Subcontracting. Subject to Section 3.3 (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 Spero for the breach of this Agreement due to breach of any subcontracting agreement by its Subcontractors. Everest hereby waives any requirement that Spero 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. Subject to Section 3.3 (Sublicense Rights), Spero may subcontract on a fee-for-service basis with a Subcontractor to perform any or all of its obligations hereunder, including by appointing one or more distributors; provided that (a) no such permitted subcontracting shall relieve Spero of any obligation hereunder (except to the extent satisfactorily performed by such Subcontractor) or any liability and Spero shall be and remain fully responsible and liable therefor, (b) the agreement pursuant to which Spero 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) Spero shall be responsible to Everest for the breach of this Agreement due to breach of any subcontracting agreement by its Subcontractors. Spero hereby waives any requirement that Everest exhaust any right, power or remedy, or proceed against any Subcontractor for any obligation or performance under this Agreement prior to proceeding directly against Spero.

3.10 Statements and Compliance with Applicable Laws. Everest shall and shall cause its Affiliates and its and their respective Sublicensees 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 Spero 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.

3.11 Section 365(n). All rights and licenses granted under or pursuant to this Agreement by Spero 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.

ARTICLE 4
GOVERNANCE

4.1 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 Spero (if Spero 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, Spero 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 Spero 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 determine any issue in a manner that would conflict with the express terms and conditions of this Agreement; or (ii) to modify or amend the terms and conditions of this Agreement.

4.2 JDC Membership and Meetings.

(a) **JDC Members.** Spero's initial JDC representatives will be [***] and Everest's initial JDC representatives will be [***]. The chairmanship for each meeting shall rotate between Spero 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 4.1 (Joint Development Committee). At this first meeting, the JDC will address the initial transfer of Licensed Know-How provided for in Section

3.5 (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 Spero 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 Spero and Everest. Each Party shall be responsible for all of its own expenses of participating in JDC meetings.

(c) **Non-Member Attendance.** Each of Spero 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 Spero 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 Spero and Everest, in which case they shall equally share such costs and expenses.

4.3 JDC Decision-Making. All decisions of the JDC shall be made by unanimous vote, with Spero'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 Spero 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 (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 Spero'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 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 Spero'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 15.10 (Dispute Resolution).

(c) If Spero does not participate in establishing the JDC or appoint members to the JDC, Everest shall have the votes and the decision-making power of Spero with respect to the JDC unless and until Spero appoints members to the JDC.

ARTICLE 5
DEVELOPMENT

5.1 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.

5.2 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 4.3 (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.

5.3 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 5.3(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**"):

A. File a CTA in the Territory for a Licensed Product within [***] years after the Effective Date;

B. Initiate a Phase 3 Clinical Trial in the Territory for a Licensed Product within [***] years after the Effective Date; and

C. 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 Spero 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 15.6 (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 thirty [***] following receipt of a First Diligence Notice, Spero may inform Everest in writing that either (i) Spero accepts the provisions of such First Diligence Notice (which Spero 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 5.3(b) (Specific Diligence Events) to incorporate a new mutually agreed Diligence Target Date or (ii) Spero 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 Spero, 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 5.3(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 Spero, 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 Spero, that it has continually used Commercially Reasonable Efforts to achieve such Diligence Milestone,

then, in addition to any other rights or remedies available to Spero, Spero may initiate termination of this Agreement pursuant to Section 12.2(b) (Termination for Cause) of this Agreement.

5.4 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 Spero 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 Spero (or its (sub)licensee) 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 Spero 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 Spero (or its (sub)licensee), Everest agrees to assist Spero (or its (sub)licensee) 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 Spero 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.

5.5 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 Spero 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 Spero to verify Everest's compliance with its obligations under this Agreement and for Spero 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 Spero shall provide the other Party with a written report summarizing in sufficient detail for Spero 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 6
REGULATORY

6.1 Regulatory Responsibilities. Everest shall be responsible, at its cost and subject to the Retained Rights and except as set forth in this ARTICLE 6, 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 Spero informed of regulatory developments related to the Compound and Licensed Products in the Licensed Field in the Territory via the JDC.

6.2 Regulatory Reports. On [***] of each year starting from the year of [***], each of Everest and Spero 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 Spero to verify Everest's compliance with its obligations under this Agreement and for Spero to properly use data and results for patent and regulatory purposes.

6.3 Regulatory Cooperation.

(a) **Everest.** Everest shall notify Spero 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 Spero 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 Spero may have sufficient opportunity to review and comment on them. Everest shall consider all comments of Spero 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 Spero, 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 Spero's Retained Rights. Material submissions made by Everest to, or correspondence with, Regulatory Authorities will be provided to Spero sufficiently in advance to enable translation by Spero, if any such submissions or correspondence are not available in English. Spero shall not provide any Regulatory Documentation of Everest, its Affiliates, or Sublicensees to any of Spero's (sub)licensees who does not agree pursuant to Section 6.3(b) (Spero) to permit its Regulatory Documentation to be shared with Everest, its Affiliates, and its Sublicensees.

(b) **Spero.** Spero shall provide or make available to Everest copies of all material Regulatory Documentation submitted or received by Spero or its Affiliates that are related to any Licensed Product outside the Territory reasonably after such submission or receipt. Spero

shall use Commercially Reasonable Efforts to negotiate an agreement with each (sub)licensee 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 (sub)licensee.

(c) **Confidentiality.** Any information of a Party to which the other Party obtains access pursuant to this Section 6.3 (Regulatory Cooperation) shall, subject to ARTICLE 11 (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 Licensed Technology to Everest under Section 3.1 (License to Everest) as to such Licensed Product shall be terminated; (2) Everest shall, at its expense, return all Spero Development Data and Spero Regulatory Documentation to Spero, as well as transfer to Spero any Everest Development Data and Everest Regulatory Documentation related to the discontinued Licensed Product; (3) the provisions of Section 2.1(e) shall apply with respect to any Assigned Patent covering such Licensed Product that Everest intends to abandon; and (4) subject to Section 2.1(e), with respect to any Everest Technology, Everest Development Data, and Everest Regulatory Documentation covering such discontinued Licensed Product, Everest shall grant a license to Spero and the provisions of Section 12.3(f) shall apply mutatis mutandis.

6.4 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 Spero, Spero 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 Spero Regulatory Documentation and the Spero Development Data to the extent necessary or reasonably useful for Everest (or such Sublicensee) 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 Spero and its Affiliates, and any current or future direct or indirect (sub)licensee of Spero 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 Spero (or such Affiliate or (sub)licensee) to Exploit the Compound, Licensed Product(s) or any product containing the Compound outside of the Territory, or (ii) in support of Spero's (or such Affiliate's or (sub)licensee'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 Spero with copies of such Everest

Development Data and Everest hereby grants to Spero 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 to such Everest Development Data independent of the requirements of Section 3.3 (Sublicense Rights); provided that, (i) each sublicense under Everest Development Data granted by Spero 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, and (ii) Spero shall be responsible to Everest for a breach of this Agreement due to the breach by such Third Party of such sublicense agreement. Spero hereby waives any requirement that Everest exhaust any right, power or remedy, or proceed against any sublicensee of Everest Development Data prior to proceeding directly against Spero. Pursuant to Section 3.3 (Sublicense Rights) and Section 3.9 (Subcontracting), Everest shall ensure that any sublicense agreement or subcontract agreement contains provisions that require Everest's current or future Sublicensees or subcontractors that generate any Regulatory Documentation or any development data (to the extent that it is not Everest Regulatory Documentation or Everest Development Data) in relation to the Development, Manufacture, Commercialize and Exploitation of Licensed Products arising from the performance of the relevant sublicense agreement or subcontract agreement relating to the Compound or a Licensed Product to make available to Spero (and its Affiliates and (sub)licensees) copies of all such Regulatory Documentation or development data solely for Spero to Develop, Manufacture, Commercialize and otherwise Exploit Licensed Products outside the Territory.

(d) Each Party will provide a signed statement to this effect, if requested by the other Party (or such Party's Affiliate, Sublicensee or (sub)licensee), 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 6.4 (Rights of Reference).

(e) Other than as expressly set forth in this Section 6.4 (Rights of Reference), nothing in this Section 6.4 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 6.4 (Rights of Reference) shall, subject to Sections 11.1 (Duty of Confidence) and 11.2 (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 6.4 (Rights of Reference) to a Regulatory Authority shall be governed by and subject to the terms of ARTICLE 11 (Confidentiality; Publication).

6.5 Recalls, Suspensions or Withdrawals. Everest shall notify Spero 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 Spero and shall consider Spero'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 6.5 (Recalls, Suspensions or Withdrawals), as between the Parties, Everest shall be solely responsible for the execution thereof. Subject to ARTICLE 14 (Indemnification; Liability), Everest shall be responsible for all costs and expenses of any such recall, market suspension or market withdrawal.

6.6 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) Spero shall establish, hold and maintain (at Spero's sole cost and expense) the global safety database for Licensed Products and (ii) Everest shall timely provide Spero with information in the possession and Control of Everest as necessary for Spero 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 Spero and at Everest's sole cost and expense.

6.7 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 Spero of such contact, inspection or notice.

ARTICLE 7
SUPPLY; MANUFACTURING

7.1 Supply Agreement.

(a) **Initial Supply Agreement**. Spero 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 Spero 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 Spero's ability to manufacture the Compound or Licensed Products in the Territory for use outside the Territory.

(b) **Commercial Supply Agreement**. Everest and Spero acknowledge and agree that, upon Completion, (i) Spero shall be no longer required to negotiate an new agreement concerning the supply of the Compound and/or the Licensed Product for Everest's Commercialization use (the "**Commercial Supply Agreement**"); and (ii) all the terms of the Original License associated with the Commercial Supply Agreement shall cease to have effect.

7.2 Manufacturing Technology Transfer. Everest and Spero acknowledge that, in order to enable Everest to Manufacture or have Manufactured the Compound and Licensed Products consistent with the terms of Section 7.3 (Manufacturing Responsibilities), upon a written request from Everest dated [***], Spero has commenced the technology transfer to Everest as follows: during a mutually agreed time period of no more than [***] days (the "**Manufacturing Transfer Period**"), Spero shall (a) make available and transfer to Everest, copies of existing embodiments of the Licensed Know-How in Spero'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 Spero 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 Spero (each, an "**Spero 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 Spero but is in the possession of a Spero CMO (and is not in Spero's possession), then during the Manufacturing Transfer Period, upon Everest's request, Spero will use Commercially Reasonable Efforts to facilitate the transfer of such Licensed Manufacturing Know-How from such Spero CMO to Everest, and/or cause such Spero 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 Spero 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, Spero 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 from and after the Effective Date under the Original Agreement or this Agreement by Spero employees or advisors to Everest under this Section 7.2 or under Section 3.5, (i) Spero 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 7.2 and Section 3.5 once such [***]-FTE threshold is used, and shall pay or reimburse Spero at the Reimbursement Rate following a written invoice in reasonable detail.

7.3 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 Spero CMO, or through another Subcontractor subject to Section 3.9 (Subcontracting). Upon request from Everest, Spero will arrange for any Spero 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 Spero CMO), then Everest will use product and manufacturing specifications and impose quality controls and assurances on itself or on such Spero CMO or such Subcontractor that are at least as stringent as those used required by Spero of its Spero CMOs and are reasonably acceptable to Spero. Everest may also request that an Spero 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 Spero with such Spero CMO. If Everest, its Affiliates, Sublicensees Manufacture, or use a Subcontractor or CMO (including a Spero 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.

7.4 Manufacturing Reports. On [***] of each year following Everest's Manufacturing of the Compound or Licensed Products, Everest shall provide Spero with a written report summarizing in sufficient detail for Spero 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.

7.5 Quality. The Parties agree that, following the Effective Date, they shall negotiate and enter into a separate Manufacturing Quality Agreement.

ARTICLE 8
COMMERCIALIZATION

8.1 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 6.5 (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.

8.2 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 [***] 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 Spero 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.

8.3 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 9
FINANCIAL PROVISIONS

9.1 Upfront Payment. Everest and Spero acknowledge that (i) Everest has paid to NPLH a one-time, non-refundable and non-creditable upfront payment of two million Dollars ($2,000,000) as required under the Original License, and (ii) Everest has [***] pursuant to the other provisions under this ARTICLE 9.

9.2 Development and Regulatory Milestone Payments. As additional consideration of the rights granted by Spero 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 Spero 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 Spero (a "**Milestone Payment**") and Spero 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 9.6 (Currency; Exchange Rate; Payments).

Development and Regulatory Milestone Events for Licensed Products	**Milestone Payments (in U.S. Dollars)**
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]

9.3 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 Spero of the achievement of

such Milestone Event and Spero shall invoice Everest for the corresponding non-refundable, non-creditable Milestone Payment set forth below and Everest shall remit payment to Spero within [***] Business Days of the receipt of such invoice, as described in Section 9.6 (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 9.3 (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 9.3 (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 Spero within [***] calendar days of such achievement. Spero shall then invoice Everest for such unpaid previous Milestone Event(s) and Everest shall pay Spero such unpaid previous milestone payment(s) within [***] Business Days of receipt of such invoice.

(d) Everest shall provide Spero with prompt written notice upon the occurrence of each Milestone Event set forth in Section 9.2 (Development and Regulatory Milestone Payments) and Section 9.3 (Commercial Milestones). In the event that, notwithstanding the fact that Everest has not given such a notice, Spero 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 9.3(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 4 (Governance) and shall be subject to resolution in accordance with Section 15.10 (Dispute Resolution). The Milestone Payments made for each Milestone Event shall be non-creditable and non-refundable.

9.4 Royalty Payments.

(a) **Royalty Rate**. In partial consideration of the rights granted by Spero to Everest hereunder, Everest, its Affiliates and/or its or their respective Sublicensees, as applicable, shall pay to Spero, 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. For clarity, the obligation to pay royalties (i) will be imposed only once with respect to the same unit of a Licensed Product and (ii) will apply to the Net Sales of Licensed Products on the terms herein irrespective of the assignment of the Assigned Patents under this Agreement and irrespective of whether such Assigned Patents are prosecuted by Spero or by Everest.

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 9.4 (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 Assigned 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's fiscal years and (ii) [***] calendar days after the last Calendar Quarter of each of Spero'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 Spero 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 Spero 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 Spero, 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.

9.5 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 9.4(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 Spero 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 9.5 (Royalty Adjustments), in the aggregate, to less than [***] percent ([***]%) of the amount otherwise payable to the Spero with respect to such Licensed Product in such jurisdiction in such Calendar Quarter in accordance with Section 9.4 (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).

9.6 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, Spero shall be paid bank wire transfer in immediately available funds to one or more bank accounts of Spero, as designated in written notice from Spero. 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.

9.7 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.

9.8 Taxes.

(a) **Taxes on Income.** Notwithstanding anything else set forth in this Section 9.8 (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 and any other payment payable by Everest to Spero 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 9.8, 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 Spero 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 Spero 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 Spero the balance when due, make timely payment to the proper taxing authority of the withheld amount and send to Spero proof of such payment to such taxing authority within [***] Business Days following such payment.

(c) **Transfer Tax**. Subject to Sections 9.8(a) (Taxes on Income) and 9.8(b) (Tax Payments) above, Everest and Spero 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 Spero ("**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 Spero 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.

9.9 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 Spero to confirm the accuracy of any royalty payments, 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 Spero and reasonably acceptable to Everest, for the sole purpose of verifying for Spero 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 Spero pursuant to this Agreement. The independent public accountant shall disclose to Spero only (x) the accuracy of Net Sales reported and the basis for royalty, Milestone Payments and any other payments made to Spero 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 Spero. No record may be audited more than once. Spero 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 Spero for the reasonable costs and expenses for such audit. Unless disputed pursuant to Section 9.10 (Audit Dispute), Everest shall pay to Spero any underpayment discovered by such audit within [***] Business Days after the accountant's report, plus interest (as set forth in Section 9.7 (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 Spero.

9.10 Audit Dispute. If Everest disputes the results of any audit conducted pursuant to Section 9.9 (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 Spero the underpayment within [***] Business Days after the Auditor's decision, plus interest (as set forth in Section 9.7 (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 Spero.

ARTICLE 10
INTELLECTUAL PROPERTY RIGHTS

10.1 Ownership of Intellectual Property

(a) **Ownership of Technology**. As between the Parties:

A. Spero shall solely own on a worldwide basis all right, title and interest in and to the Licensed Know-How with respect to any and all Spero Sole Inventions, and

B. 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 3.1 (Licenses

to Everest) and 3.2 (License to Spero)) 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:

A. in the Territory, Everest shall be the sole and exclusive owner of all the rights, title and interest in and to any and all Joint Inventions and Joint Invention Patents;

B. outside the Territory, each of Spero and Everest shall own an equal, undivided interest in any and all Joint Inventions and Joint Invention Patents; and

C. Each of Spero 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 3.1 (License to Everest) and Section 3.2 (License to Spero), each of Spero 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 Amendment 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 Spero 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 10.1(a) (Ownership of Technology) or 10.1(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 12.3 (Effect of Termination) and Section 6.3(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) Spero 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, Spero shall retain all right, title and interest in and to its Corporate Names.

(g) **Ownership of Development Data**. Subject to ARTICLE 3 (Licenses), Section 6.3(d) (Discontinuation) and Section 12.3 (Effect of Termination), Everest shall own Everest Development Data and Spero shall own Spero Development Data.

10.2 Patent Prosecution and Maintenance.

(a) Subject to Section 10.2(b), Spero 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 Assigned 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). Spero 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, Spero 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. Spero 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 Spero if [***] Business Days is not practicable given the filing deadline) of receiving the draft filings and correspondence from Spero. The costs and expenses of such preparation, filing, prosecution and maintenance of the Assigned Patents, Joint Patents and Everest Patents shall be shared by Spero and Everest such that Spero shall be responsible for the costs and expenses of such preparation, filing, prosecution and maintenance of 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 Assigned Patents, Joint Patents and Everest Patents in the Territory. For the avoidance of doubt, Spero shall be responsible for all costs incurred prior to the Effective Date with respect to the prosecution and maintenance of any Assigned Patents. If Everest reasonably determines that an Assigned Patent added after the Amendment Effective Date (other than Patent Rights added by an In-License Agreement that Everest has accepted pursuant to Section 3.4(b)A (In-License Agreements)) or a Joint Patent, in either case, is of low value to Everest, then Everest shall promptly notify Spero, in which case, following delivery of such notice to Spero, Everest shall no longer be obligated to pay for any costs and expenses of preparation, filing, prosecution and maintenance of such Assigned Patent or Joint Patent, as the case may be.

(b) Notwithstanding the provisions of Section 10.2(a), upon Everest's request at any time, Spero shall immediately transfer any and all files relating to the preparation, filing, prosecution (including any interferences, reissue proceedings and reexaminations) and maintenance of all the Everest Patents in the Territory (including but not limited to (Assigned Patents) to Everest such that Everest, through counsel of its own choice, controls the preparation, filing, prosecution and maintenance of all the Everest Patents in the Territory. Under such circumstances, Everest shall be responsible for all the costs and expenses related thereto. Everest shall consult with Spero and keep Spero reasonably informed of the status of the Assigned Patents in the Territory and shall promptly provide Spero with all material correspondence received from any patent authority in the Territory in connection therewith. In addition, Everest shall promptly provide Spero with drafts of all proposed material filings and correspondence to any patent authority in the Territory with respect to the Assigned Patents for Spero's review and comment prior to the submission of such proposed filings and correspondence. Everest shall confer with Spero and consider in good faith Spero's comments prior to submitting such filings and correspondence relating to the Assigned Patents, provided that Spero provides such comments within [***] Business Days (or a shorter period reasonably designated by Everest if [***] Business Days is not practicable given the filing deadline) of receiving such draft filings and correspondence from Everest.

(c) Subject to the provisions of Section 6.3(d) (Discontinuation), in the event that Spero desires to abandon or cease prosecution or maintenance of any Assigned Patent, Joint Patent or Everest Patent in the Territory (or any jurisdiction therein), Spero 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 Spero, Everest shall have the right to assume prosecution and maintenance of such Assigned 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 Spero, Spero 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).

10.3 Cooperation of the Parties. Each Party agrees to cooperate fully in the preparation, filing, prosecution and maintenance of Patents under Section 10.2 (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 10.2 (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.

10.4 Infringement by Third Parties.

(a) **Notice.** In the event that either Spero or Everest becomes aware of any infringement or threatened infringement by a Third Party of any Assigned Patent in the Territory

or any Joint Patent in 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 Spero 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 or outside the Territory of an application for a product referencing a Licensed Product, or any declaratory judgment or equivalent action challenging any Assigned Patent in the Territory or Joint Patent in or outside 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 Assigned Patents and Joint Patents**

A. If such Product Infringement is occurring solely in the Territory, Everest shall have the first right, as between Spero 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 Assigned Patent or Joint Patent, at its own expense and by counsel of its own choice. Spero 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 Spero 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 Assigned 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, Spero 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 in the Territory of any Assigned 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 Spero, 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) Spero's lost Milestone Payments and royalty payments that would otherwise be payable to Spero 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 Assigned 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 9.4 (Royalty Payments) and the commercial Milestone Payment obligations under Section 9.3 (Commercial Milestones).

B. If such Product Infringement is occurring solely outside the Territory, Spero shall have the first right, as between Spero 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 outside the Territory of any 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 by counsel of its own choice, and Spero and its counsel will reasonably cooperate with Everest and its counsel in strategizing, preparing and prosecuting any such action or proceeding. If Spero fails to bring an action or proceeding outside the Territory with respect to such Product Infringement of any 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 outside the Territory at its own expense and by counsel of its own choice, and Spero 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 outside the Territory of any 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 Spero, 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) Spero's (or its (sub)licensee'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 9.4 (Royalty Payments) and the commercial Milestone Payment obligations under Section 9.3 (Commercial Milestones).

(c) **Cooperation.** In the event a Party brings an action in accordance with this Section 10.4 (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**. Spero 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 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 such infringement of any 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.

10.5 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 10.4(b) (Enforcement of Assigned 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 14 (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) Spero 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) Spero 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 10.5 (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 Spero for its reasonable and verifiable out-of-pocket costs and expenses incurred in connection therewith; (d) Everest shall keep Spero reasonably informed of all material developments in connection with any such claim, suit or proceeding; (e) Everest agrees to provide Spero with copies of all material pleadings filed in such action and to allow Spero 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 10.5 (Infringement Claims by Third Parties) shall be borne by Everest subject to ARTICLE 14 (Indemnification; Liability).

10.6 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 Assigned Patents, Joint Patents or Everest Patents worldwide, by a Third Party and of which such Party becomes aware. As between the Parties: (a) Spero shall have the first right, but not the obligation, to defend and control the defense of the validity and enforceability of any Joint Patents outside the Territory, at its sole cost and expense, using counsel of Spero's choice; and (b) Everest shall have the first right, but not the obligation, to defend and control the defense of the validity and enforceability of the Assigned Patents, Everest Patents worldwide, or Joint Patents in the Territory at its sole cost and expense, using counsel of Everest's choice. For purposes of this Section 10.6 (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 under this Section 10.6 (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 least [***] 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 10.6 (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 any Patents licensed under Section 3.1 (License to Everest) or Section 3.2 (License to Spero), 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.

10.7 Consent for Settlement. Neither Party shall unilaterally enter into any settlement or compromise of any action or proceeding under this ARTICLE 10 (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.

10.8 Common Ownership under Joint Research Agreement. Notwithstanding anything to the contrary in this ARTICLE 10, no Party shall have the right to make an election under 35 U.S.C. 102(c) when exercising its rights under this ARTICLE 10 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).

10.9 Patent Extensions. Spero 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 Assigned 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 expense. If the Parties cannot agree, the matter will be referred to the JDC for decision pursuant to Section 4.3 (JDC Decision Making).

10.10 Trademarks. Spero 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.

10.11 Spero Trademarks. If Everest is lawfully required by any Regulatory Authority to use any of the Spero Trademarks or any other Trademark used by Spero 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 Spero, and Spero 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.

10.12 Patent Challenges by Spero.

(a) If Spero or any of its Affiliates commences a Challenge to the validity or enforceability of any Assigned Patents or Everest Patents, unless Spero or such Affiliate dismisses or withdraws such legal action within [***] days of commencing such Challenge, then Everest shall (i) not be required to make any remaining payment under ARTICLE 9 and (ii) have the right to terminate this Agreement pursuant to Section 12.2(c).

(b) If Spero or any of its Affiliates participates in a Challenge commenced by any other person or entity to the validity or enforceability of any Assigned Patents or Everest Patents, unless Spero or such Affiliate withdraws from such legal action within [***] days of participation in such Challenge, then Everest shall (i) not be required to make any remaining payment under ARTICLE 9 and (ii) have the right to terminate this Agreement pursuant to Section 12.2(c).

(c) If any sublicensee of Spero or any of its Affiliates, 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 Assigned Patents or Everest Patents, unless such sublicensee withdraws from such legal action within [***] days of written notice from Everest to Spero, then (i) Everest shall have the right to terminate this Agreement pursuant to Section 12.2(c) and (ii) the obligation of Everest to make any remaining payments to Spero under ARTICLE 9 shall be suspended until such Challenge is either settled by the parties or finally determined by a court, arbitrator, patent office or other Government Authority of competent jurisdiction, in each case from which no appeal can be taken, or from which no appeal was taken within the allowable time period (such settlement or final determination, a "**Challenge Resolution**"). Once a Challenge Resolution has occurred, then, on a jurisdiction-by-jurisdiction and Licensed Product-by-Licensed Product, the following provisions shall, if Everest has not terminated this Agreement as a result of such Challenge, apply with respect to the suspension of such payments to Spero:

A. If Everest prevailed on the merits of such Challenge and Everest is, as a result of such Challenge Resolution, not required to (x) license any Patents in any jurisdiction, (y) make any payments of any type to any Person that participated in such Challenge, including payments in respect of Net Sales of a Licensed Product in any jurisdiction in the Territory, and (z) lower the selling price of any Licensed Product in any jurisdiction in the Territory, then the obligation of Everest to make such remaining payments to Spero under ARTICLE 9 shall be reinstated, retroactive to the date of such suspension; provided that Everest shall be permitted to deduct and offset from such payment obligations under ARTICLE 9 the actual out-of-pocket costs to Everest (evidence of which shall be furnished to Spero in reasonable written detail at the time of such deduction and offset) of defending such Challenge (collectively, the "**Challenge Defense Costs**") and

B. If the Persons participating in such Challenge prevail, in whole or in part, on the merits of such Challenge and, as a result of such Challenge Resolution, Everest is required to (x) license any Patents in any jurisdiction in the Territory, (y) make any payments of any type to any Person that participated in such Challenge, including payments in respect of Net Sales of a Licensed Product in any jurisdiction in the Territory, or (z) lower the selling price of any Licensed Product in any jurisdiction in the Territory, then the obligation of Everest to make such remaining payments to Spero under ARTICLE 9 shall be reinstated, retroactive to the date of such suspension; provided that (1) Everest shall be permitted to deduct and offset from such payment obligations the following, without duplication of any such deduction and offset: (A) the Challenge Defense Costs; (B) the amounts paid to any Person participating in such Challenge in respect of a license to any Patents in any jurisdiction in the Territory that Everest was required to obtain as a result of such Challenge Resolution (evidence of which payments shall be furnished to Spero in reasonable written detail at the time of such deduction and offset); and (C) the payments of any type to a Person that participated in such Challenge, including payments in respect of Net Sales of a Licensed Product in any jurisdiction in the Territory (evidence of which shall be furnished to Spero in reasonable written detail at the time of such deduction and offset); and (2) if Everest is required to lower the selling price of any Licensed Product in any jurisdiction in the Territory, then Everest shall only be required to make royalty payments hereunder, if any, on Net Sales of such Licensed Product in such jurisdiction in the Territory at such lower selling price as if such selling price were reduced as of the date of such Challenge.

C. For clarity, if Everest does deduct and offset any Challenge Defense Costs under this 10.12 (Patent Challenges by Spero) then such Challenge Defense Costs shall not constitute a Claim for which Everest or any Everest Indemnitee may seek indemnification pursuant to ARTICLE 14ARTICLE 14.

ARTICLE 11
CONFIDENTIALITY; PUBLICATION

11.1 Duty of Confidence. Subject to the other provisions of this ARTICLE 11 (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 11 (Confidentiality; Publication).

11.2 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.

11.3 Authorized Disclosures. Notwithstanding the obligations set forth in Section 11.1 (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) or (sub)licensees (in the case of Spero), 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 11 (Confidentiality; Publication);

(f) to actual or potential investors, investment bankers, lenders, other financing sources, collaborators 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 11 (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.

11.4 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 Spero no later than [***] Business Days prior to the planned submission for publication or presentation for Spero's comment. Everest shall: (a) consider in good faith any comments thereto provided by Spero within such [***] day period; and (b) remove any Confidential Information of Spero if requested by Spero. Spero 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 Spero delivered pursuant to Section 15.9. Spero may reasonably request a reasonable delay in publication or presentation in order to protect patentable

information. If Spero 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 Spero to file patent applications protecting Spero's rights in such information.

11.5 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 11.5 (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.

11.6 Reporting of Financial Information. From and after the Amendment 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 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 Amendment 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'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 Spero any proposed filing containing or incorporating by reference any financial statements provided to Everest under this Section 11.6 (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 Spero a reasonable opportunity to comment thereon and (ii) in good faith consider incorporating such comments. Everest shall reimburse Spero for all costs and expenses incurred by or on account of Spero in connection with its compliance with this Section 11.6 (Reporting of Financial Information). All information of Spero obtained by or on behalf of Everest under this Section 11.6 (Reporting of Financial Information) shall be deemed Confidential Information of Spero.

11.7 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 11 (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

Spero 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 Assigned 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 11.7(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 11.7 (Privileged Communications).

ARTICLE 12
TERM AND TERMINATION

12.1 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 3.1 (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 3.1 (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 3.2 (License to Spero) 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.

12.2 Termination.

(a) **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 Spero, 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.

(b) **Termination for Cause.** If either Spero 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 12.2(b) (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 15.10 (Dispute Resolution) with respect to the alleged breach, which stay and tolling shall continue until such dispute has been resolved in accordance with Section 15.10 (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).

(c) **Termination for Patent Challenge.** Without affecting Everest's right to suspend, offset or be exempted from remaining payments to Spero pursuant to Section 10.12, Everest may terminate this Agreement upon [***] days' prior written notice to Spero if Spero 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 Assigned Patents or Everest Patents, unless Spero, such Affiliate or sublicensee dismisses or withdraws such legal action within [***] days of commencing or participation in such Challenge. Spero 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 Patents Controlled by Spero, unless Everest, such Affiliate or Sublicensee dismisses or withdraws such legal action within [***] days of commencing or participation in such Challenge.

(d) **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.

12.3 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 3.1 (License to Everest) shall terminate;

(b) If this Agreement is terminated by Everest pursuant to Section 12.2(a) (Termination by Everest for Convenience), or by Spero pursuant to Section 12.2(b) (Termination for Cause), 12.2(b) (Termination for Patent Challenge) or 12.2(d) (Termination for Bankruptcy),

Spero shall have an exclusive option to acquire back the Assigned Patents pursuant to Section 12.2(b);

(c) If this Agreement is terminated by Spero pursuant to Section 12.2(b) (Termination for Cause), 12.2(b) (Termination for Patent Challenge) or 12.2(d) (Termination for Bankruptcy), Everest hereby grants to Spero, effective 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.

(d) If this Agreement is terminated by Everest pursuant to Section 12.2(d) (Termination for Bankruptcy), then Spero hereby grants to Everest, effective only upon such termination, an exclusive (even as to Spero), royalty-free, fully-paid, perpetual and irrevocable license, with the right to grant sublicenses through multiple tiers, under the Licensed Technology, Spero Development Data and Spero's Regulatory Documentation, to Develop, make, have made, use, import, offer for sale, sell and otherwise Commercialize or Exploit the Compound and Licensed Products in the Territory in the Licensed Field.

(e) If this Agreement is terminated by Everest pursuant to Section 12.2(b) (Termination for Cause), or 12.2(d) (Termination for Bankruptcy), then Spero 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 Spero 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 Spero under Section 3.2 (License to Spero) shall terminate. If such agreement is reached, then such license agreement shall include, among other things, the following provisions:

A. Spero, 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 Spero, 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 [***]:

Calendar Year Net Sales (in Dollars) for [***] in the Territory	**Royalty Rates as a Percentage (%) of Net Sales**
[***]	[***]%
[***]	[***]%

B. Provisions substantially similar to those contained in Sections 9.5 (Royalty Adjustments) through 9.10 (Audit Dispute) shall also be included in such license agreement.

(f) If this Agreement is terminated by Everest pursuant to Section 12.2(a) (Termination by Everest for Convenience), then Spero may, within [***] days of termination, request that Everest enter into a license agreement with Spero, in which case Spero 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 Spero 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

A. Spero, 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 Spero, 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 [***]:

Calendar Year Net Sales (in Dollars) for [***] in the Territory	**Royalty Rates as a Percentage (%) of Net Sales**
[***]	[***]%
[***]	[***]%

B. Provisions substantially similar to those contained in Sections 9.5 (Royalty Adjustments) through 9.10 (Audit Dispute) shall also be included in such license agreement.

(g) Spero 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.

(h) Everest shall return to Spero or destroy, at Spero's election, all Confidential Information of Spero, including all copies thereof and all materials, substances and compositions delivered or provided by or on behalf of Spero to Everest.

(i) Everest shall deliver to Spero 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 12.3(f) (Effect of Termination - subsection (f)) above.

(j) Everest shall disclose to Spero all Everest Know-How, Everest Development Data and all Joint Inventions to the extent not already known to Spero, which may be necessary or reasonably useful for Spero to continue to Develop, Manufacture and Commercialize the Compound and Licensed Products in the Licensed Field. In addition, Everest shall, at Spero'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 Spero or its designee.

(k) 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 Spero, with Spero 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 11 (Confidentiality; Publication).

(l) Everest shall, at Spero's request and election, use Commercially Reasonable Efforts to facilitate negotiations between Spero and Everest's Third Party providers of clinical research, manufacturing and/or distribution services and to assign any contracts with such entities to Spero.

(m) Everest shall, and shall cause its Affiliates and its and their Sublicensees to, promptly provide a copy to Spero of all Licensed Product Agreements, and, to the extent requested by Spero in writing, use reasonable efforts to assign to Spero 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 Spero in all reasonable respects to secure the consent of the applicable Third Party to such assignment, at Everest's expense;

(n) Everest shall transfer to Spero all units of the Compound and the Licensed Products in its possession, provided that Spero shall reimburse Everest for the Cost of Goods of such units.

(o) Everest shall, and hereby does, effective on such termination, assign to Spero 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.

12.4 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 6.4 (Rights of Reference), Section 9.8 (Taxes), Section 9.9 (Financial Records and Audit), Section 9.10 (Audit Dispute), Section 10.1 (Ownership of Intellectual Property), ARTICLE 11 (Confidentiality; Publicity), Section 12.3 (Effect of Termination), this Section 12.4 (Survival), ARTICLE 14 (Indemnification; Liability), and ARTICLE 15 (General Provisions) hereof shall survive the expiration or termination of this Agreement.

In addition, in the event that this Agreement is terminated by Everest pursuant to Section 12.2(b) (Termination for Cause) and, pursuant to Section 12.3 (Effect of Termination), either Spero does not timely request that Everest enter into good faith negotiations concerning the terms of an agreement with Everest granting Spero a license under the Everest Technology and Everest Development Data, or if no agreement is timely reached, then, the provisions of Sections 10.2 through 10.9 of ARTICLE 10 (Intellectual Property), solely with respect to Joint Inventions, shall also survive the expiration or termination of this Agreement.

12.5 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 13
REPRESENTATIONS AND WARRANTIES

13.1 Representations and Warranties of Each Party. Each Party represents and warrants to each other Parties as of the Amendment 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.

13.2 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:

A. 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.

B. 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 Amendment 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).

C. 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.

D. 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 Spero, in a manner that is inconsistent with the exclusive license granted to Everest under Section 3.1 (Licenses to Everest) or (B) Everest Technology, in the case of Everest, in a manner that is inconsistent with the exclusive license granted to Spero under Section 3.2 (License to Spero), in each case without the prior written consent of the other Party (which consent shall not be unreasonably withheld, conditioned or delayed)

E. Each Party shall not grant any right to any Third Party under the (A) Licensed Technology (in the case of Spero) 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 Spero hereunder.

13.3 Representations and Warranties by Spero. Spero represents and warrants to Everest as of the Amendment Effective Date that:

(a) to Spero's knowledge, the patents and patent applications listed on Exhibit A constitute all Assigned Patents existing as of the Amendment Effective Date;

(b) Spero 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, to assign the Assigned Patents, and grant the license under the Licensed Technology, to Everest as purported to be granted under this Agreement;

(c) Spero has not previously assigned, transferred, conveyed or otherwise encumbered its right, title and interest in any Assigned Patent or Licensed Technology in a manner that is inconsistent with the assignment to Everest under Section 2.1 or the exclusive license granted to Everest under Section 3.1 (Licenses to Everest), other than encumbrances constituting Permitted Liens.

(d) The Assigned Patents and Licensed Technology are 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 Assigned Patents and 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 Spero provided to Everest for evaluation and (ii) IND(s) submitted to the applicable Regulatory Authority(ies).

(e) Spero has not received any notice from a Third Party that the Development of the Compound or any Licensed Product conducted by Spero prior to the Amendment Effective Date has infringed any Patents of any Third Party or infringed or misappropriated any other intellectual property of any Third Party. Based on Spero's understanding as of the Amendment Effective Date of the Compound and the Licensed Products and their intended use as of the Amendment 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 Spero, (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 Spero'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) Spero has not as of the Amendment Effective Date granted any right to any Third Party under any Assigned Patents or Licensed Technology that would conflict with the rights granted to Everest hereunder;

(g) Spero has no knowledge as of the Amendment Effective Date of any Third Party that is infringing or misappropriating any of the Assigned Patents or Licensed Technology;

(h) no claim or action has been brought or, to Spero's knowledge, threatened in writing by any Third Party alleging that the issued patents in the Assigned 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 Assigned Patents for which the U.S. federal government retains rights as identified in Section 3.1(b) (Licenses to Everest - subsection (b)), Spero 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 Assigned Patents to Everest as provided under 3.1 (Licenses to Everest);

(j) to Spero's knowledge, as of the Amendment Effective Date, there is no Know-How owned or controlled by Spero that is necessary for the Development of the Compound that is not within the Licensed Know-How; and

(k) to Spero's knowledge, (x) all clinical trials conducted by Spero or its Affiliates prior to the Amendment 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 Amendment Effective Date has, or is reasonably expected to have, any materially negative impact on the Exploitation of any Licensed Product in the Territory.

13.4 Representations and Warranties by Everest. Everest represents and warrants to Spero as of the Amendment 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 Spero under Section 3.2 (License to Spero);

(b) Everest has not as of the Amendment 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 Spero hereunder;

(c) Everest has no knowledge as of the Amendment 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 Amendment 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 Amendment 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 Spero hereunder.

13.5 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 14
INDEMNIFICATION; LIABILITY

14.1 Indemnification by Spero. Spero 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 Spero of this Agreement (other than a breach of Section 13.3(d));

(b) the gross negligence or willful misconduct on the part of Spero 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 Spero 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 Spero pursuant to Section 14.2 (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, Spero 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 Spero or any Affiliate.

14.2 Indemnification by Everest. Everest shall indemnify, defend and hold Spero, its Affiliates, and their respective officers, directors, agents and employees ("**Spero 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 Spero has an obligation to indemnify Everest pursuant to Section 14.1 (Indemnification by Spero) hereof or, to the extent such Claims result from the material breach by Spero of any covenant, representation (other than the representation set forth in Section 13.3(d), warranty or other agreement made by Spero in this Agreement or the negligence or willful misconduct of any Spero Indemnitee. Notwithstanding the above, Everest will have no obligation to defend or indemnify Spero or its Affiliates for any claim brought by a shareholder or a class of shareholders of Spero 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.

14.3 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 14 (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 14.3(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 14 (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 14.3(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 14.3(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 14.3(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.

14.4 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 14 (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.

14.5 Special, Indirect and Other Losses. EXCEPT IN THE EVENT OF A BREACH OF SECTION 3.7 (NON-DIVERSION), SECTION 3.8 (NON-COMPETE) OR ARTICLE 11 (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 14.5 shall not be construed to limit either Party's indemnification obligations under Section 14.1 (Indemnification by Spero) or Section 14.2 (Indemnification by Everest), as applicable.

14.6 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 15
GENERAL PROVISIONS

15.1 Governing Law. This Agreement shall be governed by and construed in accordance with the law of [***].

15.2 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 15.2 (Assignment) shall be null and void.

(b) The rights to Information, materials and intellectual property:

A. 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

B. 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.

15.3 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 Spero and Everest; provided that, pursuant to the definition of "Spero Trademarks" herein, Spero may designate in a writing to Everest from time to time such other Trademarks, names and logos as Spero, 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.

15.4 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.

15.5 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.

15.6 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, pandemics, 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.

15.7 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. Spero hereby undertakes to use Commercially Reasonable Efforts to obtain necessary licenses (if required) for exporting the Compound, the Licensed Products, the Assigned Patents and the Licensed Technology from the United States or other countries.

15.8 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.

15.9 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 **Spero**:

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**:

F66, Tower 1, Plaza 66
West Nanjing Road 1266
Shanghai 200040, PRC
Attention: George Qiao
Fax: [***]

With a copy to:

Morrison & Foerster
Suite 4401, HKRI Centre One, HKRI Taikoo Hui
288 Shimen Road (No. 1)
Shanghai 200041, P.R. China
Attention: Chuan Sun
Facsimile: [***]

15.10 Dispute Resolution.

(a) Except as provided in Section 4.3(a) or Excluded Claims as set forth in subsection 15.10(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 4.3 (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 15.10(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 15.10(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 [***] 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 14.5 (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, patent application, trademark or copyright, and no such claim shall be subject to arbitration pursuant to subsections (b) and (c) of this Section 15.10 (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.

15.11 Performance by Affiliates. Each Party may discharge any obligations and exercise any rights hereunder through any of its Affiliates. 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.

15.12 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.

15.13 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.

15.14 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.

15.15 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

15.16 No Benefit to Third Parties. Except as provided in ARTICLE 14 (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.

15.17 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.

15.18 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 Agreement to be executed by their duly authorized representatives.

Everest Medicines II Limited

By:	/s/ Kerry Levan Blanchard
Name:	Kerry Levan Blanchard
Title:	CEO
Date:	07-Jan-2021

Spero Therapeutics, Inc.

By:	/s/ Ankit Mahadevia
Name:	Ankit Mahadevia
Title:	CEO
Date:	1/15/2021

Solely for the purpose of Section 3.3(e)

Spero Potentiator, Inc.

By:	/s/ Ankit Mahadevia
Name:	Ankit Mahadevia
Title:	CEO
Date:	1/15/2021

LIST OF EXHIBITS

Exhibit A: Assigned Patents Existing as of the Amendment Effective Date

Reference	Territory	Application No.	Publication No.	Status	Filing Date	Assignee
[***]						
[***]	[***]	[***]	[***]	[***]	[***]	[***]
	[***]	[***]	[***]	[***]	[***]	[***]
	[***]	[***]	[***]	[***]	[***]	[***]
	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]
	[***]	[***]	[***]	[***]	[***]	[***]
	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]

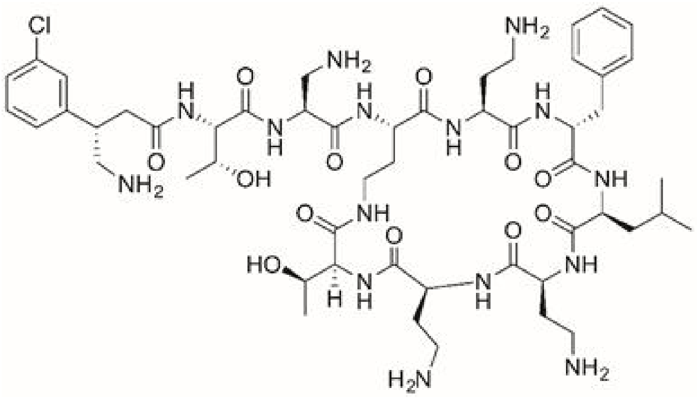
[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

Exhibit B: Spero Trademarks

Spero Reference	Mark	Country	Classes	Status	Appl. No.	Appl. Date	Reg. No.	Reg. Date
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]	[***]

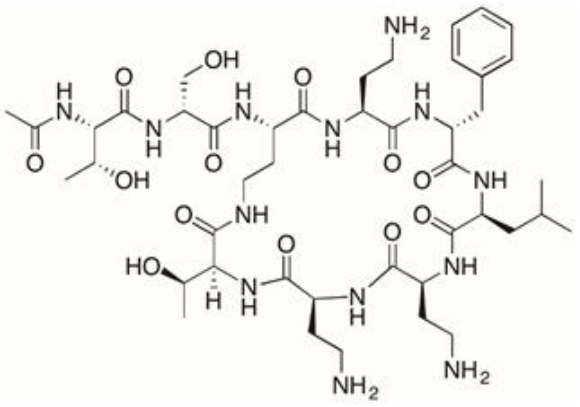
[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

Exhibit C: SPR206



[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

Exhibit D: SPR741



[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

Exhibit E: Development Plan as of Amendment Effective Date

[***]

[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

Exhibit 10.28

Spero Therapeutics, Inc.
Shares of Common Stock
(par value $0.001 per share)

Controlled Equity Offering℠

Sales Agreement

March 11, 2021

Cantor Fitzgerald & Co.
499 Park Avenue
New York, NY 10022

Ladies and Gentlemen:

Spero Therapeutics, Inc., a Delaware corporation (the "**Company**"), confirms its agreement (this "**Agreement**") with Cantor Fitzgerald & Co. (the "**Agent**"), as follows:

1. Issuance and Sale of Shares. The Company agrees that, from time to time during the term of this Agreement, on the terms and subject to the conditions set forth herein, it may issue and sell through the Agent, shares of common stock (the "**Placement Shares**") of the Company, par value $0.001 per share (the "**Common Stock**"); *provided*, *however*, that in no event shall the Company issue or sell through the Agent such number or dollar amount of Placement Shares that would (a) exceed the number or dollar amount of shares of Common Stock registered on the effective Registration Statement (as defined below) pursuant to which the offering is being made, (b) exceed the number of authorized but unissued shares of Common Stock (less shares of Common Stock issuable upon exercise, conversion or exchange of any outstanding securities of the Company or otherwise reserved from the Company's authorized capital stock), (c) exceed the number or dollar amount of shares of Common Stock permitted to be sold under Form S-3 (including General Instruction I.B.6 thereof, if applicable) or (d) exceed the number or dollar amount of shares of Common Stock for which the Company has filed a Prospectus Supplement (as defined below) (the lesser of (a), (b), (c) and (d), the "**Maximum Amount**"). Notwithstanding anything to the contrary contained herein, the parties hereto agree that compliance with the limitations set forth in this Section 1 on the amount of Placement Shares issued and sold under this Agreement shall be the sole responsibility of the Company and that the Agent shall have no obligation in connection with such compliance. The offer and sale of Placement Shares through the Agent will be effected pursuant to the Registration Statement filed by the Company and which will be declared effective by the Securities and Exchange Commission (the "**Commission**"), although nothing in this Agreement shall be construed as requiring the Company to use the Registration Statement to issue Common Stock.

The Company has filed or will file, in accordance with the provisions of the Securities Act of 1933, as amended (the "**Securities Act**"), and the rules and regulations thereunder (the "**Securities Act Regulations**"), with the Commission a registration statement on Form S-3, including a base prospectus, relating to certain securities, including the Placement Shares to be

issued from time to time by the Company, and which incorporates by reference documents that the Company has filed or will file in accordance with the provisions of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), and the rules and regulations thereunder (the "**Exchange Act Regulations**"). The Company has prepared a prospectus or a prospectus supplement to the base prospectus included as part of the registration statement, which prospectus or prospectus supplement relates to the Placement Shares to be issued from time to time by the Company (the "**Prospectus Supplement**"). The Company will furnish to the Agent, for use by the Agent, copies of the prospectus included as part of such registration statement, as supplemented, by the Prospectus Supplement, relating to the Placement Shares to be issued from time to time by the Company. The Company may file one or more additional registration statements from time to time that will contain a base prospectus and related prospectus or prospectus supplement, if applicable (which shall be a Prospectus Supplement), with respect to the Placement Shares. Except where the context otherwise requires, such registration statement(s), including all documents filed as part thereof or incorporated by reference therein, and including any information contained in a Prospectus (as defined below) subsequently filed with the Commission pursuant to Rule 424(b) under the Securities Act Regulations or deemed to be a part of such registration statement pursuant to Rule 430B of the Securities Act Regulations, is herein called the "**Registration Statement**." The base prospectus or base prospectuses, including all documents incorporated therein by reference, included in the Registration Statement, as it may be supplemented, if necessary, by the Prospectus Supplement, in the form in which such prospectus or prospectuses and/or Prospectus Supplement have most recently been filed by the Company with the Commission pursuant to Rule 424(b) under the Securities Act Regulations, together with the then issued Issuer Free Writing Prospectus(es) (as defined below), is herein called the "**Prospectus**."

Any reference herein to the Registration Statement, any Prospectus Supplement, Prospectus or any Issuer Free Writing Prospectus shall be deemed to refer to and include the documents, if any, incorporated by reference therein (the "**Incorporated Documents**"), including, unless the context otherwise requires, the documents, if any, filed as exhibits to such Incorporated Documents. Any reference herein to the terms "amend," "amendment" or "supplement" with respect to the Registration Statement, any Prospectus Supplement, the Prospectus or any Issuer Free Writing Prospectus shall be deemed to refer to and include the filing of any document under the Exchange Act on or after the most-recent effective date of the Registration Statement, or the date of the Prospectus Supplement, Prospectus or such Issuer Free Writing Prospectus, as the case may be, and incorporated therein by reference. For purposes of this Agreement, all references to the Registration Statement, the Prospectus or to any amendment or supplement thereto shall be deemed to include the most recent copy filed with the Commission pursuant to its Electronic Data Gathering Analysis and Retrieval system, or if applicable, the Interactive Data Electronic Application system when used by the Commission (collectively, "**EDGAR**").

The Company and the Agent hereby agree that, effective as of such time as the Commission declares effective the Registration Statement filed by the Company on the date hereof, the Controlled Equity Offering Sales Agreement, dated December 3, 2018, by and between the Company and the Agent shall automatically terminate and be of no further force or effect, other than those provisions set forth therein that survive termination of the Agreement pursuant to the terms thereof.

2. Placements. Each time that the Company wishes to issue and sell Placement Shares hereunder (each, a "**Placement**"), it will notify the Agent by email notice (or other method mutually agreed to by the parties) of the number of Placement Shares to be issued, the time period during which sales are requested to be made, any limitation on the number of Placement Shares that may be sold in any one day and any minimum price below which sales may not be made (a "**Placement Notice**"), the form of which is attached hereto as Schedule 1. The Placement Notice shall originate from any of the individuals from the Company set forth on Schedule 3 (with a copy to each of the other individuals from the Company listed on such schedule), and shall be addressed to each of the individuals from the Agent set forth on Schedule 3, as such Schedule 3 may be amended from time to time. The Placement Notice shall be effective unless and until (i) the Agent declines to accept the terms contained therein for any reason, in its sole discretion, provided the Agent delivers written notice thereof to the Company within two (2) Business Days (as defined below) after receipt of such Placement Notice, (ii) the entire amount of the Placement Shares thereunder have been sold, (iii) the Company suspends or terminates the Placement Notice or (iv) this Agreement has been terminated under the provisions of Section 12. The amount of any discount, commission or other compensation to be paid by the Company to the Agent in connection with the sale of the Placement Shares shall be calculated in accordance with the terms set forth in Schedule 2. It is expressly acknowledged and agreed that neither the Company nor the Agent will have any obligation whatsoever with respect to a Placement or any Placement Shares unless and until the Company delivers a Placement Notice to the Agent and the Agent does not decline such Placement Notice pursuant to the terms set forth above, and then only upon the terms specified therein and herein. In the event of a conflict between the terms of this Agreement and the terms of a Placement Notice, the terms of the Placement Notice will control.

3. Sale of Placement Shares by the Agent. Subject to the provisions of Section 5(a), the Agent, for the period specified in the Placement Notice, will use its commercially reasonable efforts consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of the Nasdaq Global Select Market (the "**Exchange**"), to sell the Placement Shares up to the amount specified in, and otherwise in accordance with the terms of, such Placement Notice. The Agent will provide written confirmation to the Company no later than the opening of the Trading Day (as defined below) immediately following the Trading Day on which it has made sales of Placement Shares hereunder setting forth the number of Placement Shares sold on such day, the compensation payable by the Company to the Agent pursuant to Section 2 with respect to such sales, and the Net Proceeds (as defined below) payable to the Company, with an itemization of the deductions made by the Agent (as set forth in Section 5(b)) from the gross proceeds that it receives from such sales. Subject to the terms of the Placement Notice, the Agent may sell Placement Shares by any method permitted by law deemed to be an "at the market offering" as defined in Rule 415(a)(4) of the Securities Act Regulations, including sales made directly on or through the Exchange or any other existing trading market for the Common Stock, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices and/or any other method permitted by law. "**Trading Day**" means any day on which Common Stock is traded on the Exchange. While a Placement Notice is in effect, neither the Agent nor any of its subsidiaries shall, for its own account, engage in (i) any short sale of any security of the Company, as defined in Regulation SHO under the Exchange Act, or (ii) any market making bidding, stabilization or other trading activity with regard to the Common Stock or related derivative securities, in each

case, if such activity would be prohibited under Regulation M under the Exchange Act or other anti-manipulation rules under the Securities Act. For the avoidance of doubt, this restriction shall not apply to transactions by or on behalf of any customer of the Agent or transactions by the Agent to facilitate any such transactions by or on behalf of any customer of the Agent.

4. Suspension of Sales. The Company or the Agent may, upon notice to the other party in writing (including by email correspondence to each of the individuals of the other party set forth on Schedule 3, if receipt of such correspondence is actually acknowledged by any of the individuals to whom the notice is sent, other than via auto-reply) or by telephone (confirmed immediately by verifiable facsimile transmission or email correspondence to each of the individuals of the other party set forth on Schedule 3), suspend any sale of Placement Shares (a "**Suspension**"); *provided*, *however*, that such Suspension shall not affect or impair any party's obligations with respect to any Placement Shares sold hereunder prior to the receipt of such notice. While a Suspension is in effect, any obligation under Sections 7(l), 7(m), and 7(n) with respect to the delivery of certificates, opinions, or comfort letters to the Agent, shall be waived. Each of the parties agrees that no such notice under this Section 4 shall be effective against any other party unless it is made to one of the individuals named on Schedule 3 hereto, as such Schedule may be amended from time to time.

5. Sale and Delivery to the Agent; Settlement.

(a) Sale of Placement Shares. On the basis of the representations and warranties herein contained and subject to the terms and conditions herein set forth, upon the Agent's acceptance of the terms of a Placement Notice, and unless the sale of the Placement Shares described therein has been declined, suspended, or otherwise terminated in accordance with the terms of this Agreement, the Agent, for the period specified in the Placement Notice, will use its commercially reasonable efforts consistent with its normal trading and sales practices and applicable law and regulations to sell such Placement Shares up to the amount specified, and otherwise in accordance with the terms of such Placement Notice. The Company acknowledges and agrees that (i) there can be no assurance that the Agent will be successful in selling Placement Shares, (ii) the Agent will incur no liability or obligation to the Company or any other person or entity ("**Person**") if it does not sell Placement Shares for any reason other than a failure by the Agent to use its commercially reasonable efforts consistent with its normal trading and sales practices and applicable law and regulations to sell such Placement Shares as required under this Agreement and (iii) the Agent shall be under no obligation to purchase Placement Shares on a principal basis pursuant to this Agreement, except as otherwise agreed by the Agent and the Company.

(b) Settlement of Placement Shares. Unless otherwise specified in the applicable Placement Notice, settlement for sales of Placement Shares will occur on the second (2nd) Trading Day (or such earlier day as is industry practice for regular-way trading) following the date on which such sales are made (each, a "**Settlement Date**"). The Agent shall notify the Company of each sale of Placement Shares no later than the opening of the Trading Day immediately following the Trading Day on which it has made sales of Placement Shares hereunder. The amount of proceeds to be delivered to the Company on a Settlement Date against receipt of the Placement Shares sold (the "**Net Proceeds**") will be equal to the aggregate sales price received by the Agent, after deduction for (i) the Agent's commission, discount or other

compensation for such sales payable by the Company pursuant to Section 2 hereof, and (ii) any transaction fees imposed by any Governmental Authority (as defined below) in respect of such sales.

(c) Delivery of Placement Shares. On or before each Settlement Date, the Company will, or will cause its transfer agent to, electronically transfer the Placement Shares being sold by crediting the Agent's or its designee's account (provided the Agent shall have given the Company written notice of such designee at least one Trading Day prior to the Settlement Date) at The Depository Trust Company through its Deposit and Withdrawal at Custodian system or by such other means of delivery as may be mutually agreed upon by the parties hereto which in all cases shall be freely tradable, transferable, registered shares in good deliverable form. On each Settlement Date, the Agent will deliver the related Net Proceeds in same day funds to an account designated by the Company on, or prior to, the Settlement Date. The Company agrees that if the Company, or its transfer agent (if applicable), defaults in its obligation to deliver Placement Shares on a Settlement Date, through no fault of the Agent, the Company agrees that in addition to and in no way limiting the rights and obligations set forth in Section 10(a) hereto, it will (i) hold the Agent harmless against any loss, claim, damage, or reasonable documented expense (including reasonable documented legal fees and expenses), as incurred, arising out of or in connection with such default by the Company or its transfer agent (if applicable) and (ii) pay to the Agent any commission, discount, or other compensation to which it would otherwise have been entitled absent such default.

(d) Denominations; Registration. Certificates for the Placement Shares, if any, shall be in such denominations and registered in such names as the Agent may request in writing at least one full Business Day before the Settlement Date. The certificates for the Placement Shares, if any, will be made available by the Company for examination and packaging by the Agent in The City of New York not later than noon (New York time) on the Business Day prior to the Settlement Date.

(e) Limitations on Offering Size. Under no circumstances shall the Company cause or request the offer or sale of any Placement Shares if, after giving effect to the sale of such Placement Shares, the aggregate gross sales proceeds of Placement Shares sold pursuant to this Agreement would exceed the lesser of (A) together with all sales of Placement Shares under this Agreement, the Maximum Amount and (B) the amount authorized from time to time to be issued and sold under this Agreement by the Company's board of directors, a duly authorized committee thereof or a duly authorized executive committee, and notified to the Agent in writing. Under no circumstances shall the Company cause or request the offer or sale of any Placement Shares pursuant to this Agreement at a price lower than the minimum price authorized from time to time by the Company's board of directors, a duly authorized committee thereof or a duly authorized executive committee, and notified to the Agent in writing. Further, under no circumstances shall the Company cause or permit the aggregate offering amount of Placement Shares sold pursuant to this Agreement to exceed the Maximum Amount.

6. Representations and Warranties of the Company. The Company represents and warrants to, and agrees with the Agent that as of the date of this Agreement and as of each Applicable Time (as defined below):

(a) Registration Statement and Prospectus. Each of the Registration Statement and any amendment thereto has or will become effective under the Securities Act. No stop order suspending the effectiveness of the Registration Statement or any post-effective amendment thereto has been issued under the Securities Act, no order preventing or suspending the use of the Prospectus has been issued and no proceedings for any of those purposes have been instituted or are pending or, to the Company's knowledge, contemplated by the Commission. The Company has complied or will comply with each request (if any) from the Commission for additional information. Each of the Registration Statement and any post-effective amendment thereto, at the time it became or will become effective, complied or will comply in all material respects with the requirements of the Securities Act and the Securities Act Regulations. The Prospectus and any amendment or supplement thereto, at the time each was filed with the Commission, complied or will comply in all material respects with the requirements of the Securities Act and the Securities Act Regulations. The Prospectus was or will be identical to the electronically transmitted copies thereof filed with the Commission pursuant to EDGAR, except to the extent permitted by Regulation S-T.

(b) Accurate Disclosure. Neither the Registration Statement nor any amendment thereto, when it became or becomes effective, contained, contains or will contain an untrue statement of a material fact or omitted, omits or will omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading. At the Applicable Time, none of (i) the Registration Statement, (ii) the Prospectus or (iii) any Issuer Free Writing Prospectus, included, includes or will include an untrue statement of a material fact or omitted, omits or will omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. Neither the Prospectus nor any amendment or supplement thereto, as of its issue date, at the time of any filing with the Commission pursuant to Rule 424(b), as of the date hereof or at the Applicable Time, included, includes or will include an untrue statement of a material fact or omitted, omits or will omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. The representations and warranties in this subsection shall not apply to statements in or omissions from the Registration Statement (or any amendment thereto) or the Prospectus (or any amendment or supplement thereto) made in reliance upon and in conformity with written information furnished to the Company by the Agent expressly for use therein. For purposes of this Agreement, the only information so furnished shall be the statements set forth in the seventh and eighth paragraphs under the caption "Plan of Distribution" in the Prospectus (collectively, the "**Agent Information**").

(c) Issuer Free Writing Prospectuses. No Issuer Free Writing Prospectus conflicts or will conflict with the information contained in the Registration Statement or the Prospectus.

(d) Company Not Ineligible Issuer. At the time of filing the Registration Statement and any post-effective amendment thereto, at the earliest time thereafter that the

Company or another offering participant made a *bona fide* offer (within the meaning of Rule 164(h)(2) of the Securities Act Regulations) of the Placement Shares and at the date hereof, the Company was not and is not an "ineligible issuer," as defined in Rule 405, without taking account of any determination by the Commission pursuant to Rule 405 that it is not necessary that the Company be considered an ineligible issuer.

(e) Emerging Growth Company Status. From the time of the initial submission of the Registration Statement to the Commission (or, if earlier, the first date on which the Company engaged directly or through any Person authorized to act on its behalf in any oral or written communication with potential investors undertaken in reliance on Section 5(d) of the Securities Act) through the date hereof, the Company has been and is an "emerging growth company," as defined in Section 2(a) of the Securities Act (an "**Emerging Growth Company**").

(f) Independent Accountants. The accountants who certified the financial statements and supporting schedules included in the Registration Statement and the Prospectus are independent public accountants with respect to the Company as required by the Securities Act, the Securities Act Regulations, the Exchange Act, the Exchange Act Regulations and the Public Company Accounting Oversight Board.

(g) Financial Statements. The financial statements included in the Registration Statement and the Prospectus, together with the related schedules and notes, present fairly, in all material respects, the financial position of the Company and its consolidated subsidiaries at the dates indicated and the statement of operations, stockholders' equity and cash flows of the Company and its consolidated subsidiaries for the periods specified; said financial statements have been prepared in conformity with U.S. generally accepted accounting principles ("**GAAP**") applied on a consistent basis throughout the periods involved, except in the case of unaudited financial statements, subject to normal year-end audit adjustments and the exclusion of certain footnotes as permitted by the applicable rules of the Commission. The supporting schedules, if any, present fairly, in all material respects, in accordance with GAAP the information required to be stated therein. The selected financial data and the summary financial information included in the Registration Statement and the Prospectus present fairly, in all material respects, the information shown therein and have been compiled on a basis consistent with that of the audited financial statements included therein. Except as included therein, no historical or pro forma financial statements or supporting schedules are required to be included or incorporated by reference in the Registration Statement or the Prospectus under the Securities Act, the Securities Act Regulations, the Exchange Act or the Exchange Act Regulations.

(h) No Material Adverse Change in Business. Except as otherwise stated therein, since the respective dates as of which information is given in the Registration Statement, the Prospectus or the Issuer Free Writing Prospectuses, if any (including any document deemed incorporated by reference therein), (A) there has been no material adverse change in the condition, financial or otherwise, or in the earnings, business affairs or business prospects of the Company and its Subsidiaries (as defined below) considered as one enterprise, whether or not arising in the ordinary course of business (a "**Material Adverse Effect**"), (B) there have been no transactions entered into by the Company or any of its Subsidiaries, other than those in the ordinary course of business, which are material with respect to the Company and its Subsidiaries

considered as one enterprise, and (C) there has been no dividend or distribution of any kind declared, paid or made by the Company on any class of its capital stock.

(i) Good Standing of the Company. The Company has been duly incorporated and is validly existing as a corporation in good standing under the laws of the State of Delaware and has corporate power and authority to own, lease and operate its properties and to conduct its business as described in the Registration Statement and the Prospectus and to enter into and perform its obligations under this Agreement; and the Company is duly qualified as a foreign corporation to transact business and is in good standing in each other jurisdiction in which such qualification is required, whether by reason of the ownership or leasing of property or the conduct of business, except where the failure so to qualify or to be in good standing would not result in a Material Adverse Effect.

(j) Good Standing of Subsidiaries. Each "significant subsidiary" of the Company (as such term is defined in Rule 1-02 of Regulation S-X) (each, a "**Subsidiary**" and, collectively, the "**Subsidiaries**") has been duly organized and is validly existing in good standing under the laws of the jurisdiction of its incorporation or organization, has corporate or similar power and authority to own, lease and operate its properties and to conduct its business as described in the Registration Statement and the Prospectus and is duly qualified to transact business and is in good standing in each jurisdiction in which such qualification is required, whether by reason of the ownership or leasing of property or the conduct of business, except where the failure to so qualify or to be in good standing would not result in a Material Adverse Effect. Except as otherwise disclosed in the Registration Statement and the Prospectus, all of the issued and outstanding capital stock of each Subsidiary has been duly authorized and validly issued, is fully paid and non-assessable and is owned by the Company, directly or through Subsidiaries, free and clear of any security interest, mortgage, pledge, lien, encumbrance, claim or equity. None of the outstanding shares of capital stock of any Subsidiary were issued in violation of the preemptive or similar rights of any securityholder of such Subsidiary. The only subsidiaries of the Company are the subsidiaries listed on Exhibit 21 to the Registration Statement.

(k) Capitalization. The Company has an authorized, issued and outstanding capitalization as set forth in the Registration Statement and the Prospectus as of the dates referred to therein (except for subsequent issuances, if any, pursuant to reservations, agreements or employee benefit plans referred to in the Registration Statement and the Prospectus or pursuant to the exercise of convertible securities or options referred to in the Registration Statement and the Prospectus). The outstanding shares of capital stock of the Company have been duly authorized and validly issued and are fully paid and non-assessable. None of the outstanding shares of capital stock of the Company were issued in violation of the preemptive or other similar rights of any securityholder of the Company.

(l) Authorization of Agreement. This Agreement has been duly authorized, executed and delivered by the Company.

(m) Authorization and Description of Placement Shares. The Placement Shares, when issued and delivered pursuant to the terms approved by the board of directors of the Company or a duly authorized committee thereof, or a duly authorized executive committee, against payment therefor as provided herein, will be duly authorized, validly issued and fully

paid and non-assessable; and the issuance of the Placement Shares will not be subject to the preemptive or other similar rights of any securityholder of the Company that have not been duly and validly waived. The Common Stock conforms, in all material respects, to all statements relating thereto contained in the Registration Statement and the Prospectus and such description conforms, in all material respects, to the rights set forth in the instruments defining the same. No holder of Placement Shares will be subject to personal liability solely by reason of being such a holder.

(n) Registration Rights. There are no persons with registration rights or other similar rights to have any securities registered for sale pursuant to the Registration Statement or otherwise registered for sale or sold by the Company under the Securities Act pursuant to this Agreement, other than those rights that have been disclosed in the Registration Statement and the Prospectus and have been waived.

(o) Absence of Violations, Defaults and Conflicts. Neither the Company nor any of its Subsidiaries is (i) in violation of its charter, by-laws or similar organizational document, (ii) in default in the performance or observance of any obligation, agreement, covenant or condition contained in any contract, indenture, mortgage, deed of trust, loan or credit agreement, note, lease or other agreement or instrument to which the Company or any of its Subsidiaries is a party or by which it or any of them is bound or to which any of the properties or assets of the Company or any Subsidiary is subject (collectively, "**Agreements and Instruments**"), except for such defaults that would not, singly or in the aggregate, result in a Material Adverse Effect, or (iii) in violation of any law, statute, rule, regulation, judgment, order, writ or decree of any arbitrator, court, governmental body, regulatory body, administrative agency or other authority, body or agency having jurisdiction over the Company or any of its Subsidiaries or any of their respective properties, assets or operations (each, a "**Governmental Entity**"), except for such violations that would not, singly or in the aggregate, result in a Material Adverse Effect. The execution, delivery and performance of this Agreement and the consummation of the transactions contemplated herein and in the Registration Statement and the Prospectus (including the issuance and sale of the Placement Shares and the use of the proceeds from the sale of the Placement Shares as described therein under the caption "Use of Proceeds") and compliance by the Company with its obligations hereunder have been duly authorized by all necessary corporate action and do not and will not, whether with or without the giving of notice or passage of time or both, conflict with or constitute a breach of, or default or Repayment Event (as defined below) under, or result in the creation or imposition of any lien, charge or encumbrance upon any properties or assets of the Company or any Subsidiary pursuant to, the Agreements and Instruments (except for such conflicts, breaches, defaults or Repayment Events or liens, charges or encumbrances that would not, singly or in the aggregate, result in a Material Adverse Effect), nor will such action result in any violation of the provisions of the charter, by-laws or similar organizational document of the Company or any of its Subsidiaries or any law, statute, rule, regulation, judgment, order, writ or decree of any Governmental Entity. As used herein, a "**Repayment Event**" means any event or condition which gives the holder of any note, debenture or other evidence of indebtedness (or any person acting on such holder's behalf) the right to require the repurchase, redemption or repayment of all or a portion of such indebtedness by the Company or any of its Subsidiaries.

(p) Absence of Labor Dispute. No labor dispute with the employees of the Company or any of its Subsidiaries exists or, to the knowledge of the Company, is imminent, and the Company is not aware of any existing or imminent labor disturbance by the employees of any of its or any Subsidiary's principal suppliers, manufacturers, customers or contractors, which, in either case, would result in a Material Adverse Effect.

(q) Absence of Proceedings. Except as disclosed in the Registration Statement and the Prospectus, there is no action, suit, proceeding, inquiry or, to the knowledge of the Company, investigation before or brought by any Governmental Entity now pending or, to the knowledge of the Company, threatened, against or affecting the Company or any of its Subsidiaries, which would result in a Material Adverse Effect, or which would materially and adversely affect their respective properties or assets or the consummation of the transactions contemplated in this Agreement or the performance by the Company of its obligations hereunder; and the aggregate of all pending legal or governmental proceedings to which the Company or any such Subsidiary is a party or of which any of their respective properties or assets is the subject which are not described in the Registration Statement and the Prospectus, including ordinary routine litigation incidental to the business, would not result in a Material Adverse Effect.

(r) Accuracy of Exhibits. There are no contracts or documents which are required to be described in the Registration Statement or the Prospectus or to be filed as exhibits to the Registration Statement which have not been so described and filed as required.

(s) Absence of Further Requirements. No filing with, or authorization, approval, consent, license, order, registration, qualification or decree of, any Governmental Entity is necessary or required for the performance by the Company of its obligations hereunder, in connection with the offering, issuance or sale of the Placement Shares hereunder or the consummation of the transactions contemplated by this Agreement, except such as have been already obtained or as may be required under the Securities Act, the Securities Act Regulations, the rules of the Exchange, state securities laws or the rules of Financial Industry Regulatory Authority ("**FINRA**").

(t) Possession of Licenses and Permits. The Company and its Subsidiaries possess such permits, certificates, licenses, approvals, clearances, registrations, exemptions, consents and other authorizations issued by the appropriate Governmental Entities necessary to conduct the business now operated by them (collectively, "**Governmental Licenses**"), including without limitation, all such Governmental Licenses required by the United States Food and Drug Administration ("**FDA**") or any component thereof and/or by any other U.S., state, local or foreign government or drug regulatory agency (collectively, the "**Regulatory Agencies**") except where the failure so to possess would not, singly or in the aggregate, result in a Material Adverse Effect. The Company and its Subsidiaries are in compliance with the terms and conditions of all Governmental Licenses, except where the failure so to comply would not, singly or in the aggregate, result in a Material Adverse Effect. All of the Governmental Licenses are valid and in full force and effect, except when the invalidity of such Governmental Licenses or the failure of such Governmental Licenses to be in full force and effect would not, singly or in the aggregate, result in a Material Adverse Effect. Each of the Company and its Subsidiaries has fulfilled and performed all of its material obligations with respect to the Governmental Licenses and, to the

Company's knowledge, no event has occurred which allows, or after notice or lapse of time would allow, revocation or termination thereof or results in any other material impairment of the rights of the holder of any Governmental License. Neither the Company nor any of its Subsidiaries has received any notice of proceedings relating to the revocation or modification of any Governmental Licenses which, singly or in the aggregate, if the subject of an unfavorable decision, ruling or finding, would result in a Material Adverse Effect.

(u) Title to Property. The Company and its Subsidiaries have good and marketable title to all real property owned by them and good title to all other properties owned by them, in each case, free and clear of all mortgages, pledges, liens, security interests, claims, restrictions or encumbrances of any kind except such as (i) are described in the Registration Statement and the Prospectus or (ii) do not, singly or in the aggregate, materially adversely affect the value of such property and do not adversely interfere with the use made and proposed to be made of such property by the Company or any of its Subsidiaries; and all of the leases and subleases material to the business of the Company and its Subsidiaries, considered as one enterprise, and under which the Company or any of its Subsidiaries holds properties described in the Registration Statement or the Prospectus, are in full force and effect, and neither the Company nor any such Subsidiary has any notice of any material claim of any sort that has been asserted by anyone adverse to the rights of the Company or any Subsidiary under any of the leases or subleases mentioned above, or affecting or questioning the rights of the Company or such Subsidiary to the continued possession of the leased or subleased premises under any such lease or sublease.

(v) Possession of Intellectual Property. The Company and its Subsidiaries own or possess, or can acquire on reasonable terms, adequate patents, patent rights, licenses, inventions, copyrights, know-how (including trade secrets and other unpatented and/or unpatentable proprietary or confidential information, systems or procedures), trademarks, service marks, trade names or other intellectual property (collectively, "**Intellectual Property**") necessary for the conduct of their respective businesses as currently conducted and as currently proposed to be conducted as disclosed in the Registration Statement and the Prospectus, now operated by them, and neither the Company nor any of its Subsidiaries has received any notice or is otherwise aware of any infringement of or conflict with asserted rights of others with respect to any Intellectual Property or of any facts or circumstances which would render any Intellectual Property invalid or inadequate to protect the interest of the Company or any of its Subsidiaries therein, and which infringement or conflict (if the subject of any unfavorable decision, ruling or finding) or invalidity or inadequacy, singly or in the aggregate, would result in a Material Adverse Effect.

(w) Regulatory Compliance. Except as described in the Registration Statement and the Prospectus, the Company and its Subsidiaries: (i) within the last five (5) years have not received any Form 483, notice of adverse finding, warning letter, untitled letter or other correspondence or written notice from any Regulatory Agency or any other Governmental Entity alleging or asserting noncompliance with any Healthcare Laws (as defined below) or the terms of any Governmental Licenses, except in each case as would not, individually or in the aggregate, have a Material Adverse Effect; (ii) have not received written notice of any claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action from any Governmental Entity or third party alleging that any product operation or activity is in violation

of any Healthcare Laws or Governmental Licenses and have no knowledge that any such Governmental Entity or third party is considering any such claim, litigation, arbitration, action, suit, investigation or proceeding, except in each case as would not, individually or in the aggregate, have a Material Adverse Effect; (iii) (A) have filed, obtained, maintained or submitted all reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by any Healthcare Laws or Governmental Licenses, (B) except as would not, individually or in the aggregate, have a Material Adverse Effect, all such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were complete and correct and not misleading on the date filed (or were corrected or supplemented by a subsequent submission), and (C) neither the Company nor its Subsidiaries is aware of any reasonable basis for any material liability with respect to such filings; and (iv) have not, and to the knowledge of the Company, the Company's officers, employees and agents have not, made any untrue statement of a material fact or fraudulent statement to any Governmental Entity or failed to disclose a material fact required to be disclosed to any Governmental Entity.

(x) Preclinical Studies and Clinical Trials. To the Company's knowledge, the descriptions of and information regarding the preclinical studies and clinical trials, and the data and results derived therefrom, contained in the Registration Statement and the Prospectus are accurate and complete in all material respects and the Company and its Subsidiaries, after due inquiry, are not aware of any nonclinical studies, clinical trials, or other information that would reasonably call into question the validity, completeness, or accuracy of any study, trial, results or data described in the Registration Statement and the Prospectus when viewed in the context in which such studies, trials, results, or data are described therein. The studies and trials conducted by or on behalf of or sponsored by the Company and its Subsidiaries were and, if still pending, are being conducted in all material respect in accordance with standard medical and scientific research procedures and all applicable laws, including, but not limited to, the Federal Food, Drug and Cosmetic Act (the "**FDCA**") and its applicable implementing regulations at 21 C.F.R. Parts 50, 54, 56, 58 and 312. Except to the extent disclosed in the Registration Statement and the Prospectus, no investigational new drug application submitted by or on behalf of the Company or its Subsidiaries with the FDA has been terminated or suspended by the FDA, and neither the FDA nor any applicable foreign regulatory agency has commenced, or, to the knowledge of the Company, threatened to initiate, any action to place a clinical hold order on, or otherwise terminate, delay or suspend, any proposed or ongoing clinical investigation conducted or proposed to be conducted by or on behalf of the Company or its Subsidiaries.

(y) Compliance with Healthcare Laws. The Company and its Subsidiaries have been in compliance in all material respects with all applicable healthcare laws, rules and regulations, to the extent they apply to the Company and its current activities, including, without limitation, (i) the FDCA (21 U.S.C. §§ 301 et seq.); (ii) all applicable foreign, federal, state and local healthcare related fraud and abuse laws, including, without limitation, the federal Anti-kickback Statute (42 U.S.C. § 1320a-7b(b)), the civil False Claims Act (31 U.S.C. §§ 3729 et seq.), the criminal False Claims Law (42 U.S.C. § 1320a-7b(a)), the civil monetary penalties law (42 U.S.C. § 1320a-7a), the exclusion laws (42 U.S.C. § 1320a-7), the Physician Payments Sunshine Act (42 U.S.C. § 1320a-7h), all criminal laws relating to healthcare fraud and abuse, including but not limited to 18 U.S.C. Sections 286, 287, 1035, 1347 and 1349, the healthcare fraud criminal provisions under the U.S. Health Insurance Portability and Accountability Act of

1996 ("**HIPAA**") (42 U.S.C. §§1320d et seq.), the Medicare statute (Title XVIII of the Social Security Act), and the Medicaid statute (Title XIX of the Social Security Act); (iii) the patient privacy, data security and beach notification provisions under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (42 U.S.C. §§17921 et seq.); (iv) comparable state and local laws; and (v) the regulations promulgated pursuant to such laws (collectively, the "**Healthcare Laws**"). Neither the Company nor any of its Subsidiaries, nor to the Company's knowledge, their officers, directors, employees, agents, have engaged in activities which are, as applicable, cause for false claims liability, civil penalties, or mandatory or permissive exclusion from Medicare, Medicaid, or any other state or federal healthcare program. Neither the Company nor any of its Subsidiaries has received written notice or other correspondence of any claim, action, suit, audit, survey, proceeding, hearing, enforcement, investigation, arbitration or other action ("**Action**") from any court, arbitrator or Governmental Entity or third party alleging that any product, operation or activity is in violation of any Healthcare Laws, and, to the Company's knowledge, no such Action is threatened. Neither the Company nor any of its Subsidiaries is a party to or has any ongoing reporting obligations pursuant to any corporate integrity agreement, deferred prosecution agreement, monitoring agreement, consent decree, settlement order, plan of correction or similar agreement with or imposed by any Governmental Entity. Additionally, neither the Company nor any of its Subsidiaries, nor any of their employees, officers or directors, or to the Company's knowledge, agents, is or has been excluded, suspended or debarred from participation in any U.S. state or federal healthcare program or human clinical research or, to the knowledge of the Company, is subject to a governmental inquiry, investigation, proceeding, or other similar action that could reasonably be expected to result in debarment, suspension, or exclusion.

(z) Environmental Laws. Except as described in the Registration Statement or the Prospectus or would not, singly or in the aggregate, result in a Material Adverse Effect, (i) neither the Company nor any of its Subsidiaries is in violation of any federal, state, local or foreign statute, law, rule, regulation, ordinance, code, policy or rule of common law or any judicial or administrative interpretation thereof, including any judicial or administrative order, consent, decree or judgment, relating to pollution or protection of human health, the environment (including, without limitation, ambient air, surface water, groundwater, land surface or subsurface strata) or wildlife, including, without limitation, laws and regulations relating to the release or threatened release of chemicals, pollutants, contaminants, wastes, toxic substances, hazardous substances, petroleum or petroleum products, asbestos-containing materials or mold (collectively, "**Hazardous Materials**") or to the manufacture, processing, distribution, use, treatment, storage, disposal, transport or handling of Hazardous Materials (collectively, "**Environmental Laws**"), (ii) the Company and its Subsidiaries have all permits, authorizations and approvals required for their operations under any applicable Environmental Laws and are each in compliance with their requirements, (iii) there are no pending or, to the knowledge of the Company, threatened administrative, regulatory or judicial actions, suits, demands, demand letters, claims, liens, notices of noncompliance or violation, investigations or proceedings relating to any Environmental Law against the Company or any of its Subsidiaries and (iv) to the knowledge of the Company, there are no events or circumstances that would reasonably be expected to form the basis of an order for clean-up or remediation, or an action, suit or proceeding by any private party or Governmental Entity, against or affecting the Company or any of its Subsidiaries relating to Hazardous Materials or any Environmental Laws.

(aa) Accounting Controls and Disclosure Controls. The Company and each of its Subsidiaries maintain effective internal control over financial reporting (as defined under Rule 13-a15 and 15d-15 under the Exchange Act Regulations and a system of internal accounting controls sufficient to provide reasonable assurances that (i) transactions are executed in accordance with management's general or specific authorization; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with GAAP and to maintain accountability for assets; (iii) access to assets is permitted only in accordance with management's general or specific authorization; and (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences. Except as described in the Registration Statement and the Prospectus, since the end of the Company's most recent audited fiscal year, there has been (A) no material weakness in the Company's internal control over financial reporting (whether or not remediated) and (B) no change in the Company's internal control over financial reporting that has materially affected, or is reasonably likely to materially adversely affect, the Company's internal control over financial reporting. The Company and each of its Subsidiaries maintain an effective system of disclosure controls and procedures (as defined in Rule 13a-15 and Rule 15d-15 under the Exchange Act Regulations) that are designed to ensure that information required to be disclosed by the 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 Commission's rules and forms, and is accumulated and communicated to the Company's management, including its principal executive officer or officers and principal financial officer or officers, as appropriate, to allow timely decisions regarding disclosure.

(bb) Compliance with the Sarbanes-Oxley Act. There is and has been no failure on the part of the Company or any of the Company's directors or officers, in their capacities as such, to comply in all material respects with any provision of the Sarbanes-Oxley Act of 2002 and the rules and regulations promulgated in connection therewith (the "**Sarbanes-Oxley Act**"), including Section 402 related to loans and Sections 302 and 906 related to certifications.

(cc) Payment of Taxes. All United States federal income tax returns of the Company and its Subsidiaries required by law to be filed have been filed and all taxes shown by such returns or otherwise assessed, which are due and payable, have been paid, except assessments against which appeals have been or will be promptly taken and as to which adequate reserves have been provided. The United States federal income tax returns of the Company through the end of its most recent fiscal year have been settled and no assessment in connection therewith has been made against the Company. The Company and its Subsidiaries have filed all other tax returns that are required to have been filed by them pursuant to applicable foreign, state, local or other law except insofar as the failure to file such returns would not result in a Material Adverse Effect, and has paid all taxes due pursuant to such returns or pursuant to any assessment received by the Company and its Subsidiaries, except for such taxes, if any, as are being contested in good faith and as to which adequate reserves have been established by the Company. The charges, accruals and reserves on the books of the Company in respect of any income and corporation tax liability for any years not finally determined are adequate to meet any assessments or re-assessments for additional income tax for any years not finally determined, except to the extent of any inadequacy that would not result in a Material Adverse Effect.

(dd) Insurance. The Company and its Subsidiaries carry or are entitled to the benefits of insurance, with financially sound and reputable insurers, in such amounts and covering such risks as is generally maintained by companies of established repute and comparable size engaged in the same or similar business, and all such insurance is in full force and effect. The Company has no reason to believe that it or any of its Subsidiaries will not be able (i) to renew its existing insurance coverage as and when such policies expire or (ii) to obtain comparable coverage from similar institutions as may be necessary or appropriate to conduct its business as now conducted and at a cost that would not result in a Material Adverse Effect. Neither of the Company nor any of its Subsidiaries has been denied any insurance coverage which it has sought or for which it has applied.

(ee) Investment Company Act. The Company is not required, and upon the issuance and sale of the Placement Shares as herein contemplated and the application of the net proceeds therefrom as described in the Registration Statement and the Prospectus will not be required, to register as an "investment company" under the Investment Company Act of 1940, as amended (the "**Investment Company Act**").

(ff) Absence of Manipulation. Neither the Company nor, to the knowledge of the Company, any affiliate of the Company has taken, nor will the Company or any affiliate take, directly or indirectly, any action which is designed, or would reasonably be expected, to cause or result in, or which constitutes, the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Placement Shares or to result in a violation of Regulation M under the Exchange Act.

(gg) Foreign Corrupt Practices Act. None of the Company, any of its Subsidiaries or, to the knowledge of the Company, any director, officer, agent, employee, affiliate or other person acting on behalf of the Company or any of its Subsidiaries is aware of or has taken any action, directly or indirectly, that would result in a violation by such persons of the Foreign Corrupt Practices Act of 1977, as amended, and the rules and regulations thereunder (the "**FCPA**"), including, without limitation, making use of the mails or any means or instrumentality of interstate commerce corruptly in furtherance of an offer, payment, promise to pay or authorization of the payment of any money, or other property, gift, promise to give, or authorization of the giving of anything of value to any "foreign official" (as such term is defined in the FCPA) or any foreign political party or official thereof or any candidate for foreign political office, in contravention of the FCPA and the Company and, to the knowledge of the Company, its affiliates have conducted their businesses in compliance with the FCPA and have instituted and maintain policies and procedures designed to ensure, and which are reasonably expected to continue to ensure, continued compliance therewith.

(hh) Money Laundering Laws. The operations of the Company and its Subsidiaries are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, the money laundering statutes of all applicable jurisdictions, the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any Governmental Entity (collectively, the "**Money Laundering Laws**"); and no action, suit or proceeding by or before any Governmental Entity involving the

Company or any of its Subsidiaries with respect to the Money Laundering Laws is pending or, to the knowledge of the Company, threatened.

(ii) OFAC. None of the Company, any of its Subsidiaries or, to the knowledge of the Company, any director, officer, agent, employee, affiliate or representative of the Company or any of its Subsidiaries is a Person currently the subject or target of any sanctions administered or enforced by the United States Government, including, without limitation, the U.S. Department of the Treasury's Office of Foreign Assets Control, the United Nations Security Council, the European Union, Her Majesty's Treasury, or other relevant sanctions authority (collectively, "**Sanctions**"), nor is the Company located, organized or resident in a country or territory that is the subject of Sanctions; and the Company will not directly or indirectly use the proceeds of the sale of the Placement Shares, or lend, contribute or otherwise make available such proceeds to any Subsidiaries, joint venture partners or other Person, to fund any activities of or business with any Person, or in any country or territory, that, at the time of such funding, is the subject of Sanctions or in any other manner that will result in a violation by any Person (including any Person participating in the transaction, whether as Agent, advisor, investor or otherwise) of Sanctions.

(jj) Lending Relationship. Except as disclosed in the Registration Statement and the Prospectus, the Company (i) does not have any material lending or other relationship with any bank or lending affiliate of the Agent and (ii) does not intend to use any of the proceeds from the sale of the Placement Shares to repay any outstanding debt owed to any affiliate of the Agent.

(kk) Statistical and Market-Related Data. Any statistical and market-related data included in the Registration Statement or the Prospectus are based on or derived from sources that the Company believes, after reasonable inquiry, to be reliable and accurate and, to the extent required, the Company has obtained the written consent to the use of such data from such sources.

(ll) Cybersecurity. The Company and its Subsidiaries' information technology assets and equipment, computers, systems, networks, hardware, software, websites, applications, and databases (collectively, "**IT Systems**") are adequate for, and operate and perform in all material respects as required in connection with the operation of the business of the Company as currently conducted, free and clear of all material bugs, errors, defects, Trojan horses, time bombs, malware and other corruptants. The Company and its Subsidiaries have implemented and maintained commercially reasonable physical, technical and administrative controls, policies, procedures, and safeguards to maintain and protect their material confidential information and the integrity, continuous operation, redundancy and security of all IT Systems and data, including all "Personal Data" (defined below) and all sensitive, confidential or regulated data ("**Confidential Data**") used in connection with their businesses. "Personal Data" means (i) a natural person's name, street address, telephone number, e-mail address, photograph, social security number or tax identification number, driver's license number, passport number, credit card number, bank information, or customer or account number; (ii) any information which would qualify as "personally identifying information" under the Federal Trade Commission Act, as amended; (iii) "personal data" as defined by the European Union General Data Protection Regulation ("**GDPR**"); (iv) any information which would qualify as "protected

health information" under the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act (collectively, "**HIPAA**"); (v) any "personal information" as defined by the California Consumer Privacy Act ("**CCPA**"); and (vi) any other piece of information that allows the identification of such natural person, or his or her family, or permits the collection or analysis of any data related to an identified person's health or sexual orientation. There have been no breaches, violations, outages or unauthorized uses of or accesses to same, except for those that have been remedied without material cost or liability or the duty to notify any other person, nor any incidents under internal review or, to the knowledge of the Company, investigations relating to the same. The Company and its Subsidiaries are presently in material compliance with all applicable laws or statutes and all judgments, orders, rules and regulations of any court or arbitrator or governmental or regulatory authority, internal policies and contractual obligations relating to the privacy and security of IT Systems, Confidential Data, and Personal Data and to the protection of such IT Systems, Confidential Data, and Personal Data from unauthorized use, access, misappropriation or modification.

(mm) Compliance with Data Privacy Laws. The Company and its Subsidiaries are, and at all times during the last three years were, in material compliance with all applicable state and federal data privacy and security laws and regulations, including without limitation HIPAA, CCPA, and GDPR (EU 2016/679) (collectively, the "**Privacy Laws**"). To ensure compliance with the Privacy Laws, the Company has in place, complies with, and takes appropriate steps to ensure compliance in all material respects with their policies and procedures relating to data privacy and security and the collection, storage, use, processing, disclosure, handling, and analysis of Personal Data and Confidential Data (the "**Policies**"). The Company has at all times made all disclosures to users or customers required by applicable laws and regulatory rules or requirements, and none of such disclosures made or contained in any Policy have been inaccurate or in violation of any applicable laws and regulatory rules or requirements in any material respect. The Company further certifies that neither it nor any Subsidiary: (i) has received notice of any actual or potential liability under or relating to, or actual or potential violation of, any of the Privacy Laws, and has no knowledge of any event or condition that would reasonably be expected to result in any such notice; (ii) is currently conducting or paying for, in whole or in part, any investigation, remediation, or other corrective action pursuant to any Privacy Law; or (iii) is a party to any order, decree, or agreement that imposes any obligation or liability under any Privacy Law.

Any certificate signed by any officer of the Company or any of its Subsidiaries and delivered to the Agent or to counsel for the Agent pursuant to or in connection with this Agreement shall be deemed to be a representation and warranty by the Company, as applicable, to the Agent as to the matters covered thereby.

7. Covenants of the Company. The Company covenants and agrees with Agent that:

(a) Registration Statement Amendments. After the date of this Agreement and during any period in which a Prospectus relating to any Placement Shares is required to be delivered by the Agent under the Securities Act (including in circumstances where such requirement may be satisfied pursuant to Rule 172 under the Securities Act or similar rule), (i) the Company will notify the Agent promptly of the time when any subsequent amendment to

the Registration Statement, other than documents incorporated by reference, has been filed with the Commission and/or has become effective or any subsequent supplement to the Prospectus has been filed and of any request by the Commission for any amendment or supplement to the Registration Statement or Prospectus or for additional information, (ii) the Company will prepare and file with the Commission, promptly upon the Agent's request, any amendments or supplements to the Registration Statement or Prospectus that, in the Agent's reasonable opinion, based on the advice of counsel, may be necessary or advisable in connection with the distribution of the Placement Shares by the Agent (*provided*, *however*, that the failure of the Agent to make such request shall not relieve the Company of any obligation or liability hereunder, or affect the Agent's right to rely on the representations and warranties made by the Company in this Agreement and *provided*, *further*, that the only remedy the Agent shall have with respect to the failure to make such filing shall be to cease making sales under this Agreement until such amendment or supplement is filed); (iii) the Company will not file any amendment or supplement to the Registration Statement or Prospectus relating to the Placement Shares or a security convertible into the Placement Shares unless a copy thereof has been submitted to the Agent within a reasonable period of time before the filing and the Agent has not reasonably objected thereto in writing within two (2) Business Days (*provided*, *however*, that the failure of the Agent to make such objection shall not relieve the Company of any obligation or liability hereunder, or affect the Agent's right to rely on the representations and warranties made by the Company in this Agreement, and the Company has no obligation to provide the Agent any advance copy of such filing or to provide the Agent an opportunity to object to such filing if such filing does not name the Agent and does not reference the transactions contemplated hereby; *provided*, *further*, that the only remedy the Agent shall have with respect to the failure by the Company to obtain such consent shall be to cease making sales under this Agreement) and the Company will furnish to the Agent at the time of filing thereof a copy of any document that upon filing is deemed to be incorporated by reference into the Registration Statement or Prospectus, except for those documents available via EDGAR; and (iv) the Company will cause each amendment or supplement to the Prospectus to be filed with the Commission as required pursuant to the applicable paragraph of Rule 424(b) of the Securities Act or, in the case of any document to be incorporated therein by reference, to be filed with the Commission as required pursuant to the Exchange Act, within the time period prescribed (the determination to file or not file any amendment or supplement with the Commission under this Section 7(a), based on the Company's reasonable opinion or reasonable objections, shall be made exclusively by the Company).

(b) Notice of Commission Stop Orders. The Company will advise the Agent, promptly after it receives notice or obtains knowledge thereof, of the issuance or threatened issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement, of the suspension of the qualification of the Placement Shares for offering or sale in any jurisdiction, or of the initiation or threatening of any proceeding for any such purpose; and it will promptly use its commercially reasonable efforts to prevent the issuance of any stop order or to obtain its withdrawal if such a stop order should be issued. The Company will advise the Agent promptly after it receives any request by the Commission for any amendments to the Registration Statement or any amendment or supplements to the Prospectus or any Issuer Free Writing Prospectus or for additional information related to the offering of the Placement Shares or for additional information related to the Registration Statement, the Prospectus or any Issuer Free Writing Prospectus; *provided*, *however*, that the Company may delay any such amendment

or supplement if, in the reasonable judgment of the Company, it is in the best interests of the Company to do so.

(c) Delivery of Prospectus; Subsequent Changes. During any period in which a Prospectus relating to the Placement Shares is required to be delivered by the Agent under the Securities Act with respect to the offer and sale of the Placement Shares (including in circumstances where such requirement may be satisfied pursuant to Rule 172 under the Securities Act or similar rule), the Company will comply in all material respects with all requirements imposed upon it by the Securities Act, as from time to time in force, and to file on or before their respective due dates all reports and any definitive proxy or information statements required to be filed by the Company with the Commission pursuant to Sections 13(a), 13(c), 14, 15(d) or any other provision of or under the Exchange Act. If the Company has omitted any information from the Registration Statement pursuant to Rule 430B under the Securities Act, it will use its best efforts to comply with the provisions of and make all requisite filings with the Commission pursuant to said Rule 430B and to notify the Agent promptly of all such filings. If during such period any event occurs as a result of which the Prospectus as then amended or supplemented would include an untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances then existing, not misleading, or if during such period it is necessary to amend or supplement the Registration Statement or Prospectus to comply with the Securities Act, the Company will promptly notify the Agent to suspend the offering of Placement Shares during such period and the Company will promptly amend or supplement the Registration Statement or Prospectus (at the expense of the Company) so as to correct such statement or omission or effect such compliance.

(d) Listing of Placement Shares. Prior to the date of the first Placement Notice, the Company will use its reasonable best efforts to cause the Placement Shares to be listed on the Exchange.

(e) Delivery of Registration Statement and Prospectus. The Company will furnish to the Agent and its counsel (at the expense of the Company) copies of the Registration Statement, the Prospectus (including all Incorporated Documents) and all amendments and supplements to the Registration Statement or Prospectus that are filed with the Commission during any period in which a Prospectus relating to the Placement Shares is required to be delivered under the Securities Act (including all documents filed with the Commission during such period that are deemed to be incorporated by reference therein), in each case as soon as reasonably practicable and in such quantities as the Agent may from time to time reasonably request and, at the Agent's request, will also furnish copies of the Prospectus to each exchange or market on which sales of the Placement Shares may be made; *provided*, *however*, that the Company shall not be required to furnish any document (other than the Prospectus) to the Agent to the extent such document is available on EDGAR.

(f) Earnings Statement. The Company will make generally available to its security holders as soon as practicable, but in any event not later than 15 months after the end of the Company's current fiscal quarter, an earnings statement covering a 12-month period that satisfies the provisions of Section 11(a) and Rule 158 of the Securities Act.

(g) Use of Proceeds. The Company will use the Net Proceeds as described in the Prospectus in the section entitled "Use of Proceeds."

(h) Notice of Other Sales. Without the prior written consent of the Agent, the Company will not, directly or indirectly, offer to sell, sell, contract to sell, grant any option to sell or otherwise dispose of any Common Stock (other than the Placement Shares offered pursuant to this Agreement) or securities convertible into or exchangeable for Common Stock, warrants or any rights to purchase or acquire, Common Stock during the period beginning on the fifth (5th) Trading Day immediately prior to the date on which any Placement Notice is delivered to the Agent hereunder and ending on the second (2nd) Trading Day immediately following the final Settlement Date with respect to Placement Shares sold pursuant to such Placement Notice (or, if the Placement Notice has been terminated or suspended prior to the sale of all Placement Shares covered by a Placement Notice, the date of such suspension or termination); and will not directly or indirectly in any other "at the market" or continuous equity transaction offer to sell, sell, contract to sell, grant any option to sell or otherwise dispose of any Common Stock (other than the Placement Shares offered pursuant to this Agreement) or securities convertible into or exchangeable for Common Stock, warrants or any rights to purchase or acquire, Common Stock prior to the later of the termination of this Agreement and the thirtieth (30th) day immediately following the final Settlement Date with respect to Placement Shares sold pursuant to such Placement Notice; *provided*, *however*, that such restrictions will not be required in connection with the Company's issuance or sale of (i) Common Stock, options to purchase Common Stock or Common Stock issuable upon the exercise of options, pursuant to any employee or director stock option or benefits plan, stock ownership plan or dividend reinvestment plan (but not Common Stock subject to a waiver to exceed plan limits in its dividend reinvestment plan) of the Company whether now in effect or hereafter implemented, (ii) Common Stock issuable upon conversion of securities or the exercise of warrants, options or other rights in effect or outstanding, and disclosed in filings by the Company available on EDGAR or otherwise in writing to the Agent and (iii) Common Stock or securities convertible into or exchangeable for shares of Common Stock as consideration for mergers, acquisitions, other business combinations or strategic alliances occurring after the date of this Agreement which are not issued for capital raising purposes.

(i) Change of Circumstances. The Company will, at any time during the pendency of a Placement Notice, advise the Agent promptly after it shall have received notice or obtained knowledge thereof, of any information or fact that would alter or affect in any material respect any opinion, certificate, letter or other document required to be provided to the Agent pursuant to this Agreement.

(j) Due Diligence Cooperation. The Company will cooperate with any reasonable due diligence review conducted by the Agent or its representatives in connection with the transactions contemplated hereby, including, without limitation, providing information and making available documents and senior corporate officers, during regular business hours and at the Company's principal offices, as the Agent may reasonably request.

(k) Required Filings Relating to Placement of Placement Shares. The Company agrees that on such dates as the Securities Act shall require, the Company will (i) file a prospectus supplement with the Commission under the applicable paragraph of Rule 424(b) under the Securities Act, which prospectus supplement will set forth, within the relevant period, the amount of Placement Shares sold through the Agent, the Net Proceeds to the Company and the compensation payable by the Company to the Agent with respect to such Placement Shares,

and (ii) deliver such number of copies of each such prospectus supplement to each exchange or market on which such sales were effected as may be required by the rules or regulations of such exchange or market.

(l) Representation Dates; Certificate. During the term of this Agreement, (1) on or prior to the date of the first Placement Notice and (2) thereafter, each time the Company:

(i) files the Prospectus relating to the Placement Shares (other than as part of any filing prior to the time of the initial effectiveness of the Registration Statement) or amends or supplements (other than a prospectus supplement relating solely to an offering of securities other than the Placement Shares) the Registration Statement or the Prospectus relating to the Placement Shares by means of a post-effective amendment, sticker, or supplement but not by means of incorporation of documents by reference into the Registration Statement or the Prospectus relating to the Placement Shares;

(ii) files an annual report on Form 10-K under the Exchange Act (including any Form 10-K/A containing amended financial information or a material amendment to the previously filed Form 10-K);

(iii) files its quarterly reports on Form 10-Q under the Exchange Act; or

(iv) files a current report on Form 8-K containing amended financial information (other than information "furnished" pursuant to Items 2.02 or 7.01 of Form 8-K or to provide disclosure pursuant to Item 8.01 of Form 8-K relating to the reclassification of certain properties as discontinued operations in accordance with Statement of Financial Accounting Standards No. 144) under the Exchange Act (each date of filing of one or more of the documents referred to in clauses (i) through (iv) shall be a "**Representation Date**");

the Company shall furnish the Agent (but in the case of clause (iv) above only if the Agent reasonably determines that the information contained in such Form 8-K is material) with a certificate dated the Representation Date, in the form attached hereto as Schedule 7(l), modified, as necessary, to relate to the Registration Statement and the Prospectus as amended or supplemented. The requirement to provide a certificate under this Section 7(l) shall be automatically waived for any Representation Date occurring (1) at a time a Suspension is in effect, which waiver shall continue until the earlier to occur of the date the Company delivers instructions for the sale of Placement Shares hereunder (which for such calendar quarter shall be considered a Representation Date) and the next occurring Representation Date and (2) at a time when no Placement Notice is pending, which waiver shall continue until the date the Company delivers a Placement Notice. Notwithstanding the foregoing, if the Company subsequently decides to sell Placement Shares following a Representation Date when the Company relied on such waiver and did not provide the Agent with a certificate under this Section 7(l), then before the Company delivers the instructions for the sale of Placement Shares or the Agent sells any Placement Shares pursuant to such instructions, the Company shall provide the Agent with a certificate in conformity with this Section 7(l) dated as of the date that the instructions for the sale of Placement Shares are issued.

(m) Legal Opinions. (1) On or prior to the date of the first Placement Notice and (2) thereafter, within five (5) Trading Days of each Representation Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 7(l) for which no waiver is applicable and excluding the date of this Agreement, the Company shall cause to be furnished to the Agent (A) a written opinion and a negative assurance letter of Mintz, Levin, Cohn, Ferris, Glovsky & Popeo, P.C. ("**Company Counsel**"), or other counsel satisfactory to the Agent, and (B) a written opinion of Cantor Colburn LLP ("**IP Counsel**"), or other counsel satisfactory to the Agent, in each case in form and substance reasonably satisfactory to Agent and its counsel, substantially similar to the forms previously provided to the Agent and its counsel, modified, as necessary, to relate to the Registration Statement and the Prospectus as then amended or supplemented; *provided*, *however*, the Company shall be required to furnish to Agent no more than one opinion from each of Company Counsel and IP Counsel hereunder per calendar quarter; and *provided*, *further*, that in lieu of such opinions for subsequent Representation Dates, counsel may furnish the Agent with a letter (a "**Reliance Letter**") to the effect that the Agent may rely on a prior opinion delivered under this Section 7(m) to the same extent as if it were dated the date of such letter (except that statements in such prior opinion shall be deemed to relate to the Registration Statement and the Prospectus as amended or supplemented as of the date of the Reliance Letter).

(n) Comfort Letter. (1) On or prior to the date of the first Placement Notice and (2) thereafter, within five (5) Trading Days of each Representation Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 7(l) for which no waiver is applicable and excluding the date of this Agreement, the Company shall cause its independent registered public accounting firm to furnish the Agent letters (the "**Comfort Letters**"), dated the date the Comfort Letter is delivered, which shall meet the requirements set forth in this Section 7(n); *provided*, *however*, that if requested by the Agent, the Company shall cause a Comfort Letter to be furnished to the Agent within ten (10) Trading Days of the date of occurrence of any material transaction or event, including the restatement of the Company's financial statements. The Comfort Letter from the Company's independent registered public accounting firm shall be in a form and substance reasonably satisfactory to the Agent, (i) confirming that they are an independent registered public accounting firm within the meaning of the Securities Act and the Public Company Accounting Oversight Board, (ii) stating, as of such date, the conclusions and findings of such firm with respect to the financial information and other matters ordinarily covered by accountants' "comfort letters" to underwriters in connection with registered public offerings (the first such letter, the "**Initial Comfort Letter**") and (iii) updating the Initial Comfort Letter with any information that would have been included in the Initial Comfort Letter had it been given on such date and modified as necessary to relate to the Registration Statement and the Prospectus, as amended and supplemented to the date of such letter.

(o) Market Activities. The Company will not, directly or indirectly, (i) take any action designed to cause or result in, or that constitutes or would reasonably be expected to constitute, the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of Common Stock or (ii) sell, bid for, or purchase Common Stock in violation of Regulation M, or pay anyone any compensation for soliciting purchases of the Placement Shares other than the Agent.

(p) Investment Company Act. The Company will conduct its affairs in such a manner so as to reasonably ensure that neither it nor any of its Subsidiaries will be or become, at any time prior to the termination of this Agreement, required to register as an "investment company," as such term is defined in the Investment Company Act.

(q) No Offer to Sell. Other than an Issuer Free Writing Prospectus approved in advance by the Company and the Agent in its capacity as agent hereunder, neither the Agent nor the Company (including its agents and representatives, other than the Agent in its capacity as such) will make, use, prepare, authorize, approve or refer to any written communication (as defined in Rule 405 under the Securities Act), required to be filed with the Commission, that constitutes an offer to sell or solicitation of an offer to buy Placement Shares hereunder.

(r) Blue Sky and Other Qualifications. The Company will use its commercially reasonable efforts, in cooperation with the Agent, to qualify the Placement Shares for offering and sale, or to obtain an exemption for the Placement Shares to be offered and sold, under the applicable securities laws of such states and other jurisdictions (domestic or foreign) as the Agent may designate and to maintain such qualifications and exemptions in effect for so long as required for the distribution of the Placement Shares (but in no event for less than one year from the date of this Agreement); *provided*, *however*, that the Company shall not be obligated to file any general consent to service of process or to qualify as a foreign corporation or as a dealer in securities in any jurisdiction in which it is not so qualified or to subject itself to taxation in respect of doing business in any jurisdiction in which it is not otherwise so subject. In each jurisdiction in which the Placement Shares have been so qualified or exempt, the Company will file such statements and reports as may be required by the laws of such jurisdiction to continue such qualification or exemption, as the case may be, in effect for so long as required for the distribution of the Placement Shares (but in no event for less than one year from the date of this Agreement).

(s) Sarbanes-Oxley Act. The Company and the Subsidiaries will maintain and keep accurate books and records reflecting their assets and maintain internal accounting controls in a manner designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP and including those policies and procedures that (i) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the Company, (ii) provide reasonable assurance that transactions are recorded as necessary to permit the preparation of the Company's consolidated financial statements in accordance with GAAP, (iii) that receipts and expenditures of the Company are being made only in accordance with management's and the Company's directors' authorization, and (iv) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on its financial statements. The Company and the Subsidiaries will maintain such controls and other procedures, including, without limitation, those required by Sections 302 and 906 of the Sarbanes-Oxley Act, and the applicable regulations thereunder that are designed to ensure that information required to be disclosed by the 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 Commission's rules and forms, including, without limitation, controls and procedures designed to ensure that information required to be disclosed by the 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 officer and principal financial officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure and to ensure that material information relating to the Company or the Subsidiaries is made known to them by others within those entities, particularly during the period in which such periodic reports are being prepared.

(t) Secretary's Certificate; Further Documentation. On or prior to the date of the first Placement Notice, the Company shall deliver to the Agent a certificate of the Secretary of the Company and attested to by an executive officer of the Company, dated as of such date, certifying as to (i) the Amended and Restated Certificate of Incorporation of the Company, (ii) the Amended and Restated Bylaws of the Company, (iii) the resolutions of the Board of Directors of the Company, or a duly authorized committee of the Board of Directors, authorizing the execution, delivery and performance of this Agreement and the issuance of the Placement Shares and (iv) the incumbency of the officers duly authorized to execute this Agreement and the other documents contemplated by this Agreement. Within five (5) Trading Days of each Representation Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 7(l) for which no waiver is applicable, the Company shall have furnished to the Agent such further information, certificates and documents as the Agent may reasonably request.

(u) Emerging Growth Company Status. The Company will promptly notify the Agent if the Company ceases to be an Emerging Growth Company at any time during the term of this Agreement.

8. Payment of Expenses. The Company will pay all expenses incident to the performance of its obligations under this Agreement, including (i) the preparation and filing of the Registration Statement, including any fees required by the Commission, and the printing or electronic delivery of the Prospectus as originally filed and of each amendment and supplement thereto, in such number as the Agent shall deem necessary, (ii) the printing and delivery to the Agent of this Agreement and such other documents as may be required in connection with the offering, purchase, sale, issuance or delivery of the Placement Shares, (iii) the preparation, issuance and delivery of the certificates, if any, for the Placement Shares to the Agent, including any stock or other transfer taxes and any capital duties, stamp duties or other duties or taxes payable upon the sale, issuance or delivery of the Placement Shares to the Agent, (iv) the fees and disbursements of the counsel, accountants and other advisors to the Company, (v) the fees and disbursements of the counsel to the Agent, payable upon the execution of this Agreement, in an amount not to exceed $50,000, (vi) the qualification or exemption of the Placement Shares under state securities laws in accordance with the provisions of Section 7(r) hereof, including filing fees, but excluding fees of the Agent's counsel, (vii) the printing and delivery to the Agent of copies of any Permitted Free Writing Prospectus (as defined below) and the Prospectus and any amendments or supplements thereto in such number as the Agent shall deem necessary, (viii) the preparation, printing and delivery to the Agent of copies of the blue sky survey, (ix) the fees and expenses of the transfer agent and registrar for the Common Stock, (x) the filing and other fees incident to any review by FINRA of the terms of the sale of the Placement Shares including the fees of the Agent's counsel (subject to the cap, set forth in clause (v) above), and

(xi) the fees and expenses incurred in connection with the listing of the Placement Shares on the Exchange.

9. Conditions to the Agent's Obligations. The obligations of the Agent hereunder with respect to a Placement will be subject to the continuing accuracy and completeness of the representations and warranties made by the Company herein, to the due performance by the Company of its obligations hereunder, to the completion by the Agent of a due diligence review satisfactory to it in its reasonable judgment, and to the continuing satisfaction (or waiver by the Agent in its sole discretion) of the following additional conditions:

(a) Registration Statement Effective. The Registration Statement shall have become effective and shall be available for the (i) resale of all Placement Shares issued to the Agent and not yet sold by the Agent and (ii) sale of all Placement Shares contemplated to be issued by any Placement Notice.

(b) No Material Notices. None of the following events shall have occurred and be continuing: (i) receipt by the Company of any request for additional information from the Commission or any other federal or state Governmental Authority during the period of effectiveness of the Registration Statement, the response to which would require any post-effective amendments or supplements to the Registration Statement or the Prospectus if such post-effective amendments or supplements have not been made and become effective; (ii) the issuance by the Commission or any other federal or state Governmental Authority of any stop order suspending the effectiveness of the Registration Statement or the initiation of any proceedings for that purpose; (iii) receipt by the Company of any notification with respect to the suspension of the qualification or exemption from qualification of any of the Placement Shares for sale in any jurisdiction or the initiation or threatening of any proceeding for such purpose; or (iv) the occurrence of any event that makes any material statement made in the Registration Statement or the Prospectus or any material document incorporated or deemed to be incorporated therein by reference untrue in any material respect or that requires the making of any changes in the Registration Statement, the Prospectus or documents so that, in the case of the Registration Statement, it will not contain an untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading and so that, in the case of the Prospectus, it will not contain an untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(c) No Misstatement or Material Omission. The Agent shall not have advised the Company that the Registration Statement or Prospectus, or any amendment or supplement thereto, contains an untrue statement of fact that in the Agent's reasonable opinion is material, or omits to state a fact that in the Agent's reasonable opinion is material and is required to be stated therein or is necessary to make the statements therein not misleading.

(d) Material Changes. Except as contemplated in the Prospectus, or disclosed in the Company's reports filed with the Commission, there shall not have been any material adverse change in the authorized capital stock of the Company or any Material Adverse Effect or any development that would reasonably be expected to cause a Material Adverse Effect, or a downgrading in or withdrawal of the rating assigned to any of the Company's securities (other than asset backed securities) by any rating organization or a public announcement by any rating

organization that it has under surveillance or review its rating of any of the Company's securities (other than asset backed securities), the effect of which, in the case of any such action by a rating organization described above, in the reasonable judgment of the Agent (without relieving the Company of any obligation or liability it may otherwise have), is so material as to make it impracticable or inadvisable to proceed with the offering of the Placement Shares on the terms and in the manner contemplated in the Prospectus.

(e) Legal Opinions. The Agent shall have received the opinion and negative assurance letter of Company Counsel and the opinion of IP Counsel required to be delivered pursuant to Section 7(m) on or before the date on which such delivery of such opinions and negative assurance letter is required pursuant to Section 7(m).

(f) Comfort Letter. The Agent shall have received the Comfort Letter required to be delivered pursuant to Section 7(n) on or before the date on which such delivery of such Comfort Letter is required pursuant to Section 7(n).

(g) Representation Certificate. The Agent shall have received the certificate required to be delivered pursuant to Section 7(l) on or before the date on which delivery of such certificate is required pursuant to Section 7(l).

(h) No Suspension. Trading in the Common Stock shall not have been suspended on the Exchange and the Common Stock shall not have been delisted from the Exchange.

(i) Other Materials. On each date on which the Company is required to deliver a certificate pursuant to Section 7(l), the Company shall have furnished to the Agent such appropriate further information, opinions, certificates, letters and other documents as the Agent may reasonably request. All such opinions, certificates, letters and other documents will be in compliance with the provisions hereof.

(j) Securities Act Filings Made. All filings with the Commission with respect to the Placement Shares required by Rule 424 under the Securities Act to have been filed prior to the issuance of any Placement Notice hereunder shall have been made within the applicable time period prescribed for such filing by Rule 424.

(k) Approval for Listing. The Placement Shares shall either have been (i) approved for listing on the Exchange, subject only to notice of issuance, or (ii) the Company shall have filed an application for listing of the Placement Shares on the Exchange at, or prior to, the issuance of any Placement Notice and the Exchange shall have reviewed such application and not provided any objections thereto.

(l) FINRA. If applicable, FINRA shall have raised no objection to the terms of this offering and the amount of compensation allowable or payable to the Agent as described in the Prospectus.

(m) No Termination Event. There shall not have occurred any event that would permit the Agent to terminate this Agreement pursuant to Section 12(a).

10. Indemnification and Contribution.

(a) Company Indemnification. The Company agrees to indemnify and hold harmless the Agent, its affiliates and their respective partners, members, directors, officers, employees and agents and each person, if any, who controls the Agent within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act as follows:

(i) against any and all loss, liability, claim, damage and expense whatsoever, as incurred, joint or several, arising out of or based upon any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement (or any amendment thereto), or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein not misleading, or arising out of any untrue statement or alleged untrue statement of a material fact included in any related Issuer Free Writing Prospectus or the Prospectus (or any amendment or supplement thereto), or the omission or alleged omission therefrom of a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading;

(ii) against any and all loss, liability, claim, damage and expense whatsoever, as incurred, joint or several, to the extent of the aggregate amount paid in settlement of any litigation, or any investigation or proceeding by any Governmental Authority, commenced or threatened, or of any claim whatsoever based upon any such untrue statement or omission, or any such alleged untrue statement or omission; *provided* that (subject to Section 10(d) below) any such settlement is effected with the written consent of the Company, which consent shall not unreasonably be delayed or withheld; and

(iii) against any and all expense whatsoever, as incurred (including the fees and disbursements of counsel), reasonably incurred in investigating, preparing or defending against any litigation, or any investigation or proceeding by any Governmental Authority, commenced or threatened, or any claim whatsoever based upon any such untrue statement or omission, or any such alleged untrue statement or omission (whether or not a party), to the extent that any such expense is not paid under (i) or (ii) above,

provided, *however*, that this indemnity agreement shall not apply to any loss, liability, claim, damage or expense to the extent arising out of any untrue statement or omission or alleged untrue statement or omission made solely in reliance upon and in conformity with the Agent Information.

(b) Agent Indemnification. The Agent agrees to indemnify and hold harmless the Company and its directors and each officer of the Company who signed the Registration Statement, and each person, if any, who controls the Company within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act against any and all loss, liability, claim, damage and expense described in the indemnity contained in Section 10(a), as incurred, but only with respect to untrue statements or omissions, or alleged untrue statements or omissions, made in the Registration Statement (or any amendments thereto), the Prospectus (or any amendment or supplement thereto) or any Issuer Free Writing Prospectus (or any amendment or supplement thereto) in reliance upon and in conformity with information relating to the Agent and furnished to the Company in writing by the Agent expressly for use therein. The Company hereby acknowledges that the only information that the Agent has furnished to the Company expressly

for use in the Registration Statement, the Prospectus or any Issuer Free Writing Prospectus (or any amendment or supplement thereto) is the Agent Information.

(c) Procedure. Any party that proposes to assert the right to be indemnified under this Section 10 will, promptly after receipt of notice of commencement of any action against such party in respect of which a claim is to be made against an indemnifying party or parties under this Section 10, notify each such indemnifying party of the commencement of such action, enclosing a copy of all papers served, but the omission so to notify such indemnifying party will not relieve the indemnifying party from (i) any liability that it might have to any indemnified party otherwise than under this Section 10 and (ii) any liability that it may have to any indemnified party under the foregoing provision of this Section 10 unless, and only to the extent that, such omission results in the forfeiture of substantive rights or defenses by the indemnifying party. If any such action is brought against any indemnified party and it notifies the indemnifying party of its commencement, the indemnifying party will be entitled to participate in and, to the extent that it elects by delivering written notice to the indemnified party promptly after receiving notice of the commencement of the action from the indemnified party, jointly with any other indemnifying party similarly notified, to assume the defense of the action, with counsel reasonably satisfactory to the indemnified party, and after notice from the indemnifying party to the indemnified party of its election to assume the defense, the indemnifying party will not be liable to the indemnified party for any legal or other expenses except as provided herein and except for the reasonable costs of investigation subsequently incurred by the indemnified party in connection with the defense. The indemnified party will have the right to employ its own counsel in any such action, but the fees, expenses and other charges of such counsel will be at the expense of such indemnified party unless (1) the employment of counsel by the indemnified party has been authorized in writing by the indemnifying party, (2) the indemnified party has reasonably concluded (based on advice of counsel) that there may be legal defenses available to it or other indemnified parties that are different from or in addition to those available to the indemnifying party, (3) a conflict or potential conflict exists (based on advice of counsel to the indemnified party) between the indemnified party and the indemnifying party (in which case the indemnifying party will not have the right to direct the defense of such action on behalf of the indemnified party) or (4) the indemnifying party has not in fact employed counsel to assume the defense of such action or counsel reasonably satisfactory to the indemnified party, in each case, within a reasonable time after receiving notice of the commencement of the action, in each of which cases the reasonable fees, disbursements and other charges of counsel will be at the expense of the indemnifying party or parties. It is understood that the indemnifying party or parties shall not, in connection with any proceeding or related proceedings in the same jurisdiction, be liable for the reasonable fees, disbursements and other charges of more than one separate firm (plus local counsel) admitted to practice in such jurisdiction at any one time for all such indemnified party or parties. All such fees, disbursements and other charges will be reimbursed by the indemnifying party promptly as they are incurred. An indemnifying party will not, in any event, be liable for any settlement of any action or claim effected without its written consent. No indemnifying party shall, without the prior written consent of each indemnified party, settle or compromise or consent to the entry of any judgment in any pending or threatened claim, action or proceeding relating to the matters contemplated by this Section 10 (whether or not any indemnified party is a party thereto), unless such settlement, compromise or consent (1) includes an express and unconditional release of each indemnified party from all liability arising out of such litigation, investigation, proceeding

or claim and (2) does not include a statement as to or an admission of fault, culpability or a failure to act by or on behalf of any indemnified party.

(d) Settlement Without Consent if Failure to Reimburse. If an indemnified party shall have requested an indemnifying party to reimburse the indemnified party for reasonable fees and expenses of counsel, such indemnifying party agrees that it shall be liable for any settlement of the nature contemplated by Section 10(a)(ii) effected without its written consent if (1) such settlement is entered into more than 45 days after receipt by such indemnifying party of the aforesaid request, (2) such indemnifying party shall have received notice of the terms of such settlement at least 30 days prior to such settlement being entered into and (3) such indemnifying party shall not have reimbursed such indemnified party in accordance with such request prior to the date of such settlement.

(e) Contribution. In order to provide for just and equitable contribution in circumstances in which the indemnification provided for in the foregoing paragraphs of this Section 10 is applicable in accordance with its terms but for any reason is held to be unavailable or insufficient from the Company or the Agent, the Company and the Agent will contribute to the total losses, claims, liabilities, expenses and damages (including any investigative, legal and other expenses reasonably incurred in connection with, and any amount paid in settlement of, any action, suit or proceeding or any claim asserted) to which the Company and the Agent may be subject in such proportion as shall be appropriate to reflect the relative benefits received by the Company on the one hand and the Agent on the other hand. The relative benefits received by the Company on the one hand and the Agent on the other hand shall be deemed to be in the same proportion as the total net proceeds from the sale of the Placement Shares (before deducting expenses) received by the Company bear to the total compensation (before deducting expenses) received by the Agent from the sale of Placement Shares on behalf of the Company. If, but only if, the allocation provided by the foregoing sentence is not permitted by applicable law, the allocation of contribution shall be made in such proportion as is appropriate to reflect not only the relative benefits referred to in the foregoing sentence but also the relative fault of the Company, on the one hand, and the Agent, on the other hand, with respect to the statements or omission that resulted in such loss, claim, liability, expense or damage, or action in respect thereof, as well as any other relevant equitable considerations with respect to such offering. Such relative fault shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or omission or alleged omission to state a material fact relates to information supplied by the Company or the Agent, the intent of the parties and their relative knowledge, access to information and opportunity to correct or prevent such statement or omission. The Company and the Agent agree that it would not be just and equitable if contributions pursuant to this Section 10(e) were to be determined by pro rata allocation or by any other method of allocation that does not take into account the equitable considerations referred to herein. The amount paid or payable by an indemnified party as a result of the loss, claim, liability, expense, or damage, or action in respect thereof, referred to above in this Section 10(e) shall be deemed to include, for the purpose of this Section 10(e), any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim to the extent consistent with Section 10(c) hereof. Notwithstanding the foregoing provisions of this Section 10(e), the Agent shall not be required to contribute any amount in excess of the commissions received by it under this Agreement and no person found guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the

Securities Act) will be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. For purposes of this Section 10(e), any person who controls a party to this Agreement within the meaning of the Securities Act, any controlled affiliates of the Agent and any officers, directors, partners, employees or agents of the Agent or any of its controlled affiliates, will have the same rights to contribution as that party, and each director of the Company and each officer of the Company who signed the Registration Statement will have the same rights to contribution as the Company, subject in each case to the provisions hereof. Any party entitled to contribution, promptly after receipt of notice of commencement of any action against such party in respect of which a claim for contribution may be made under this Section 10(e), will notify any such party or parties from whom contribution may be sought, but the omission to so notify will not relieve that party or parties from whom contribution may be sought from any other obligation it or they may have under this Section 10(e) except to the extent that the failure to so notify such other party materially prejudiced the substantive rights or defenses of the party from whom contribution is sought. Except for a settlement entered into pursuant to the last sentence of Section 10(c) hereof, no party will be liable for contribution with respect to any action or claim settled without its written consent if such consent is required pursuant to Section 10(c) hereof.

11. Representations and Agreements to Survive Delivery. The indemnity and contribution agreements contained in Section 10 of this Agreement and all representations and warranties of the Company herein or in certificates delivered pursuant hereto shall survive, as of their respective dates, regardless of (i) any investigation made by or on behalf of the Agent, any controlling persons, or the Company (or any of their respective officers, directors, employees or controlling persons), (ii) delivery and acceptance of the Placement Shares and payment therefor or (iii) any termination of this Agreement.

12. Termination.

(a) The Agent may terminate this Agreement, by notice to the Company, as hereinafter specified at any time (1) if there has been, since the time of execution of this Agreement or since the date as of which information is given in the Prospectus, any change, or any development or event involving a prospective change, in the condition, financial or otherwise, or in the business, properties, earnings, results of operations or prospects of the Company and its Subsidiaries considered as one enterprise, whether or not arising in the ordinary course of business, which individually or in the aggregate, in the sole judgment of the Agent is material and adverse and makes it impractical or inadvisable to market the Placement Shares or to enforce contracts for the sale of the Placement Shares, (2) if there has occurred any material adverse change in the financial markets in the United States or the international financial markets, any outbreak of hostilities or escalation thereof or other calamity or crisis or any change or development involving a prospective change in national or international political, financial or economic conditions, in each case the effect of which is such as to make it, in the judgment of the Agent, impracticable or inadvisable to market the Placement Shares or to enforce contracts for the sale of the Placement Shares, (3) if trading in the Common Stock has been suspended or limited by the Commission or the Exchange, or if trading generally on the Exchange has been suspended or limited, or minimum prices for trading have been fixed on the Exchange, (4) if any suspension of trading of any securities of the Company on any exchange or in the over-the-counter market shall have occurred and be continuing, (5) if a major disruption of securities

settlements or clearance services in the United States shall have occurred and be continuing, or (6) if a banking moratorium has been declared by either U.S. Federal or New York authorities. Any such termination shall be without liability of any party to any other party except that the provisions of Section 8 (Payment of Expenses), Section 10 (Indemnification and Contribution), Section 11 (Representations and Agreements to Survive Delivery), Section 17 (Governing Law and Time; Waiver of Jury Trial) and Section 18 (Consent to Jurisdiction) hereof shall remain in full force and effect notwithstanding such termination. If the Agent elects to terminate this Agreement as provided in this Section 12(a), the Agent shall provide the required notice as specified in Section 13 (Notices).

(b) The Company shall have the right, by giving ten (10) days' notice as hereinafter specified to terminate this Agreement in its sole discretion at any time after the date of this Agreement. Any such termination shall be without liability of any party to any other party except that the provisions of Section 8, Section 10, Section 11, Section 17 and Section 18 hereof shall remain in full force and effect notwithstanding such termination.

(c) The Agent shall have the right, by giving ten (10) days' notice as hereinafter specified to terminate this Agreement in its sole discretion at any time after the date of this Agreement. Any such termination shall be without liability of any party to any other party except that the provisions of Section 8, Section 10, Section 11, Section 17 and Section 18 hereof shall remain in full force and effect notwithstanding such termination.

(d) Unless earlier terminated pursuant to this Section 12, this Agreement shall automatically terminate upon the issuance and sale of all of the Placement Shares on the terms and subject to the conditions set forth herein except that the provisions of Section 8, Section 10, Section 11, Section 17 and Section 18 hereof shall remain in full force and effect notwithstanding such termination.

(e) This Agreement shall remain in full force and effect unless terminated pursuant to Sections 12(a), (b), (c) or (d) above or otherwise by mutual agreement of the parties; *provided*, *however*, that any such termination by mutual agreement shall in all cases be deemed to provide that Section 8, Section 10, Section 11, Section 17 and Section 18 shall remain in full force and effect.

(f) Any termination of this Agreement shall be effective on the date specified in such notice of termination; *provided*, *however*, that such termination shall not be effective until the close of business on the date of receipt of such notice by the Agent or the Company, as the case may be. If such termination shall occur prior to the Settlement Date for any sale of Placement Shares, such Placement Shares shall settle in accordance with the provisions of this Agreement.

13. Notices. All notices or other communications required or permitted to be given by any party to any other party pursuant to the terms of this Agreement shall be in writing, unless otherwise specified, and if sent to the Agent, shall be delivered to:

Cantor Fitzgerald & Co.
499 Park Avenue
New York, NY 10022
Attention: Capital Markets
Facsimile: (212) 307-3730

with copies to:

Cantor Fitzgerald & Co.
499 Park Avenue
New York, NY 10022
Attention: General Counsel
Facsimile: (212) 829-4708

and a copy to:

Latham & Watkins LLP
12670 High Bluff Drive
San Diego, CA 92130
Attention: Michael E. Sullivan, Esq.
Facsimile: (858) 523-5450

and if to the Company, shall be delivered to:

Spero Therapeutics, Inc.
675 Massachusetts Avenue, 14th Floor
Cambridge, MA 02139
Attention: Tamara Joseph, Esq., Chief Legal Officer

with a copy to:

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
One Financial Center
Boston, MA 02111
Attention: Matthew J. Gardella
Facsimile: (617) 542-2241

Each party to this Agreement may change such address for notices by sending to the parties to this Agreement written notice of a new address for such purpose. Each such notice or other communication shall be deemed given (i) when delivered personally or by verifiable facsimile transmission (with an original to follow) on or before 4:30 p.m., New York City time, on a Business Day or, if such day is not a Business Day, on the next succeeding Business Day, (ii) by Electronic Notice as set forth in the next paragraph, (iii) on the next Business Day after timely delivery to a nationally-recognized overnight courier or (iv) on the Business Day actually

received if deposited in the U.S. mail (certified or registered mail, return receipt requested, postage prepaid). For purposes of this Agreement, "**Business Day**" shall mean any day on which the Exchange and commercial banks in the City of New York are open for business.

An electronic communication ("**Electronic Notice**") shall be deemed written notice for purposes of this Section 13 if sent to the electronic mail address specified by the receiving party under separate cover. Electronic Notice shall be deemed received at the time the party sending Electronic Notice receives verification of receipt by the receiving party. Any party receiving Electronic Notice may request and shall be entitled to receive the notice on paper, in a nonelectronic form ("**Nonelectronic Notice**") which shall be sent to the requesting party within ten (10) days of receipt of the written request for Nonelectronic Notice.

14. Successors and Assigns. This Agreement shall inure to the benefit of and be binding upon the Company and the Agent and their respective successors and the parties referred to in Section 10 hereof. References to any of the parties contained in this Agreement shall be deemed to include the successors and permitted assigns of such party. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and permitted assigns any rights, remedies, obligations or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement. Neither party may assign its rights or obligations under this Agreement without the prior written consent of the other party; *provided*, *however*, that the Agent may assign its rights and obligations hereunder to an affiliate thereof without obtaining the Company's consent, so long as such affiliate is a registered broker-dealer and the Agent provides advanced notice of such assignment to the Company.

15. Adjustments for Stock Splits. The parties acknowledge and agree that all share-related numbers contained in this Agreement shall be adjusted to take into account any stock split, stock dividend or similar event effected with respect to the Placement Shares.

16. Entire Agreement; Amendment; Severability; Waiver. This Agreement (including all schedules and exhibits attached hereto and Placement Notices issued pursuant hereto) constitutes the entire agreement and supersedes all other prior and contemporaneous agreements and undertakings, both written and oral, among the parties hereto with regard to the subject matter hereof. Neither this Agreement nor any term hereof may be amended except pursuant to a written instrument executed by the Company and the Agent. In the event that any one or more of the provisions contained herein, or the application thereof in any circumstance, is held invalid, illegal or unenforceable as written by a court of competent jurisdiction, then such provision shall be given full force and effect to the fullest possible extent that it is valid, legal and enforceable, and the remainder of the terms and provisions herein shall be construed as if such invalid, illegal or unenforceable term or provision was not contained herein, but only to the extent that giving effect to such provision and the remainder of the terms and provisions hereof shall be in accordance with the intent of the parties as reflected in this Agreement. No implied waiver by a party shall arise in the absence of a waiver in writing signed by such party. No failure or delay in exercising any right, power, or privilege hereunder shall operate as a waiver thereof, nor shall any single or partial exercise thereof preclude any other or further exercise thereof or the exercise of any right, power, or privilege hereunder.

17. **GOVERNING LAW AND TIME; WAIVER OF JURY TRIAL. THIS AGREEMENT SHALL BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF THE STATE OF NEW YORK WITHOUT REGARD TO THE PRINCIPLES OF CONFLICTS OF LAWS. SPECIFIED TIMES OF DAY REFER TO NEW YORK CITY TIME. EACH PARTY HEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF OR RELATING TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY.**

18. **CONSENT TO JURISDICTION. EACH PARTY HEREBY IRREVOCABLY SUBMITS TO THE EXCLUSIVE JURISDICTION OF THE STATE AND FEDERAL COURTS SITTING IN THE CITY OF NEW YORK, BOROUGH OF MANHATTAN, FOR THE ADJUDICATION OF ANY DISPUTE HEREUNDER OR IN CONNECTION WITH ANY TRANSACTION CONTEMPLATED HEREBY, AND HEREBY IRREVOCABLY WAIVES, AND AGREES NOT TO ASSERT IN ANY SUIT, ACTION OR PROCEEDING, ANY CLAIM THAT IT IS NOT PERSONALLY SUBJECT TO THE JURISDICTION OF ANY SUCH COURT, THAT SUCH SUIT, ACTION OR PROCEEDING IS BROUGHT IN AN INCONVENIENT FORUM OR THAT THE VENUE OF SUCH SUIT, ACTION OR PROCEEDING IS IMPROPER. EACH PARTY HEREBY IRREVOCABLY WAIVES PERSONAL SERVICE OF PROCESS AND CONSENTS TO PROCESS BEING SERVED IN ANY SUCH SUIT, ACTION OR PROCEEDING BY MAILING A COPY THEREOF (CERTIFIED OR REGISTERED MAIL, RETURN RECEIPT REQUESTED) TO SUCH PARTY AT THE ADDRESS IN EFFECT FOR NOTICES TO IT UNDER THIS AGREEMENT AND AGREES THAT SUCH SERVICE SHALL CONSTITUTE GOOD AND SUFFICIENT SERVICE OF PROCESS AND NOTICE THEREOF. NOTHING CONTAINED HEREIN SHALL BE DEEMED TO LIMIT IN ANY WAY ANY RIGHT TO SERVE PROCESS IN ANY MANNER PERMITTED BY LAW.**

19. 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. Delivery of an executed Agreement by one party to the other may be made by facsimile or electronic transmission.

20. Construction. The section and exhibit headings herein are for convenience only and shall not affect the construction hereof. References herein to any law, statute, ordinance, code, regulation, rule or other requirement of any Governmental Authority shall be deemed to refer to such law, statute, ordinance, code, regulation, rule or other requirement of any Governmental Authority as amended, reenacted, supplemented or superseded in whole or in part and in effect from time to time and also to all rules and regulations promulgated thereunder.

21. Permitted Free Writing Prospectuses. The Company represents, warrants and agrees that, unless it obtains the prior written consent of the Agent, which consent shall not be unreasonably withheld, condition or delayed, and the Agent represents, warrants and agrees that, unless it obtains the prior written consent of the Company, which consent shall not be unreasonably withheld, condition or delayed, it has not made and will not make any offer

relating to the Placement Shares that would constitute an Issuer Free Writing Prospectus, or that would otherwise constitute a "free writing prospectus," as defined in Rule 405, required to be filed with the Commission. Any such free writing prospectus consented to by the Agent or by the Company, as the case may be, is hereinafter referred to as a "Permitted Free Writing Prospectus." The Company represents and warrants that it has treated and agrees that it will treat each Permitted Free Writing Prospectus as an "issuer free writing prospectus," as defined in Rule 433, and has complied and will comply with the requirements of Rule 433 applicable to any Permitted Free Writing Prospectus, including timely filing with the Commission where required, legending and record keeping. For the purposes of clarity, the parties hereto agree that all free writing prospectuses, if any, listed in Exhibit 21 hereto are Permitted Free Writing Prospectuses.

22. Absence of Fiduciary Relationship. The Company acknowledges and agrees that:

(a) the Agent is acting solely as agent in connection with the public offering of the Placement Shares and in connection with each transaction contemplated by this Agreement and the process leading to such transactions, and no fiduciary or advisory relationship between the Company or any of its respective affiliates, stockholders (or other equity holders), creditors or employees or any other party, on the one hand, and the Agent, on the other hand, has been or will be created in respect of any of the transactions contemplated by this Agreement, irrespective of whether or not the Agent has advised or is advising the Company on other matters, and the Agent has no obligation to the Company with respect to the transactions contemplated by this Agreement except the obligations expressly set forth in this Agreement;

(b) it is capable of evaluating and understanding, and understands and accepts, the terms, risks and conditions of the transactions contemplated by this Agreement;

(c) neither the Agent nor its affiliates have provided any legal, accounting, regulatory or tax advice with respect to the transactions contemplated by this Agreement and it has consulted its own legal, accounting, regulatory and tax advisors to the extent it has deemed appropriate;

(d) it is aware that the Agent and its affiliates are engaged in a broad range of transactions which may involve interests that differ from those of the Company and the Agent and its affiliates have no obligation to disclose such interests and transactions to the Company by virtue of any fiduciary, advisory or agency relationship or otherwise; and

(e) it waives, to the fullest extent permitted by law, any claims it may have against the Agent or its affiliates for breach of fiduciary duty or alleged breach of fiduciary duty in connection with the sale of Placement Shares under this Agreement and agrees that the Agent and its affiliates shall not have any liability (whether direct or indirect, in contract, tort or otherwise) to it in respect of such a fiduciary duty claim or to any person asserting a fiduciary duty claim on its behalf or in right of it or the Company, employees or creditors of Company.

23. Definitions. As used in this Agreement, the following terms have the respective meanings set forth below:

"**Applicable Time**" means (i) each Representation Date and (ii) the time of each sale of any Placement Shares pursuant to this Agreement.

"**Governmental Authority**" means (i) any federal, provincial, state, local, municipal, national or international government or governmental authority, regulatory or administrative agency, governmental commission, department, board, bureau, agency or instrumentality, court, tribunal, arbitrator or arbitral body (public or private); (ii) any self-regulatory organization; or (iii) any political subdivision of any of the foregoing.

"**Issuer Free Writing Prospectus**" means any "issuer free writing prospectus," as defined in Rule 433, relating to the Placement Shares that (1) is required to be filed with the Commission by the Company, (2) is a "road show" that is a "written communication" within the meaning of Rule 433(d)(8)(i) whether or not required to be filed with the Commission, or (3) is exempt from filing pursuant to Rule 433(d)(5)(i) because it contains a description of the Placement Shares or of the offering that does not reflect the final terms, in each case in the form filed or required to be filed with the Commission or, if not required to be filed, in the form retained in the Company's records pursuant to Rule 433(g) under the Securities Act Regulations.

"**Rule 164**," "**Rule 172**," "**Rule 405**," "**Rule 415**," "**Rule 424**," "**Rule 424(b)**," "**Rule 430B**," and "**Rule 433**" refer to such rules under the Securities Act Regulations.

All references in this Agreement to financial statements and schedules and other information that is "contained," "included" or "stated" in the Registration Statement or the Prospectus (and all other references of like import) shall be deemed to mean and include all such financial statements and schedules and other information that is incorporated by reference in the Registration Statement or the Prospectus, as the case may be.

All references in this Agreement to the Registration Statement, the Prospectus or any amendment or supplement to any of the foregoing shall be deemed to include the copy filed with the Commission pursuant to EDGAR; all references in this Agreement to any Issuer Free Writing Prospectus (other than any Issuer Free Writing Prospectuses that, pursuant to Rule 433, are not required to be filed with the Commission) shall be deemed to include the copy thereof filed with the Commission pursuant to EDGAR; and all references in this Agreement to "supplements" to the Prospectus shall include, without limitation, any supplements, "wrappers" or similar materials prepared in connection with any offering, sale or private placement of any Placement Shares by the Agent outside of the United States.

[***Signature Page Follows***]

If the foregoing correctly sets forth the understanding between the Company and the Agent, please so indicate in the space provided below for that purpose, whereupon this letter shall constitute a binding agreement between the Company and the Agent.

Very truly yours,

SPERO THERAPEUTICS, INC.

By: /s/ Ankit Mahadevia, M.D.
Name: Ankit Mahadevia, M.D.
Title: President and Chief Executive Officer

ACCEPTED as of the date first-above written:

CANTOR FITZGERALD & CO.

By: /s/ Sage Kelly
Name: Sage Kelly
Title: Senior Managing Director, Head of Investment Banking

SCHEDULE 1

Form of Placement Notice

From: Spero Therapeutics, Inc.

To: Cantor Fitzgerald & Co.
Attention:_____

Subject: Placement Notice

Date:

Ladies and Gentlemen:

Pursuant to the terms and subject to the conditions contained in the Sales Agreement between Spero Therapeutics, Inc., a Delaware corporation (the "**Company**"), and Cantor Fitzgerald & Co. ("**Agent**"), dated March 11, 2021, the Company hereby requests that the Agent sell up to [•] of the Company's common stock, par value $0.001 per share, at a minimum market price of $[•] per share, during the time period beginning [month, day, time] and ending [month, day, time].

Spero Therapeutics, Inc.

[Name, Title]

cc: [other Spero notice parties]

SCHEDULE 2

Compensation

The Company shall pay to the Agent in cash, upon each sale of Placement Shares pursuant to this Agreement, an amount equal to 3.0% of the aggregate gross proceeds from each sale of Placement Shares.

SCHEDULE 3

Notice Parties

The Company

Ankit Mahadevia, Chief Executive Officer

Sath Shukla, Chief Financial Officer

The Agent

Sameer Vasudev (svasudev@cantor.com)

Controlled Equity Offering Group (CFCEO@cantor.com)

SCHEDULE 7(l)

Form of Representation Date Certificate Pursuant to Section 7(l)

The undersigned, the duly qualified and elected [•], of Spero Therapeutics, Inc., a Delaware corporation (the "Company"), does hereby certify in such capacity and on behalf of the Company, pursuant to Section 7(l) of the Sales Agreement, dated March 11, 2021 (the "Sales Agreement"), between the Company and Cantor Fitzgerald & Co., that to the best of the knowledge of the undersigned:

(i) The representations and warranties of the Company in Section 6 of the Sales Agreement (A) to the extent such representations and warranties are subject to qualifications and exceptions contained therein relating to materiality or Material Adverse Effect, are true and correct on and as of the date hereof with the same force and effect as if expressly made on and as of the date hereof, except for those representations and warranties that speak solely as of a specific date and which were true and correct as of such date, and (B) to the extent such representations and warranties are not subject to any qualifications or exceptions, are true and correct in all material respects as of the date hereof as if made on and as of the date hereof, except for those representations and warranties that speak solely as of a specific date and which were true and correct in all material respects as of such date; *provided*, *however*, that such representations and warranties also shall be qualified by the disclosure included or incorporated by reference in the Registration Statement and Prospectus; and

(ii) The Company has complied with all agreements and satisfied all conditions on its part to be performed or satisfied pursuant to the Sales Agreement at or prior to the date hereof.

Capitalized terms used herein without definition shall have the meanings given to such terms in the Sales Agreement.

SPERO THERAPEUTICS, INC.

By: _____

Name: _____

Title: _____

Date: [•]

Form of Legal Opinion Pursuant to Section 7(m)

Exhibit 21

Permitted Free Writing Prospectus

None.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-228661) and Form S-8 (Nos. 333-230283, 333-230281, 333-222060, 333-237283, and 333-241681) of Spero Therapeutics, Inc. of our report dated March 11, 2021 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 11, 2021

Exhibit 31.1

CERTIFICATIONS UNDER SECTION 302

I, Ankit Mahadevia, M.D., certify that:

1. I have reviewed this annual report on Form 10-K of Spero Therapeutics, Inc.;

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

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

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

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

b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

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

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

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

Date: March 11, 2021

/s/ Ankit Mahadevia, M.D.
Ankit Mahadevia, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS UNDER SECTION 302

I, Satyavrat Shukla, 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 11, 2021

/s/ Satyavrat Shukla
Satyavrat Shukla
Chief Financial Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer)

Exhibit 32

CERTIFICATIONS UNDER SECTION 906

Pursuant to section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), each of the undersigned officers of Spero Therapeutics, Inc., a Delaware corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report for the year ended December 31, 2020 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 11, 2021

/s/ Ankit Mahadevia, M.D.
Ankit Mahadevia, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Dated: March 11, 2021

/s/ Satyavrat Shukla
Satyavrat Shukla
Chief Financial Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer)