SPERO THERAPEUTICS

Spero Therapeutics is committed to advancing new therapies for patients with rare diseases and multidrug-resistant (MDR) bacterial infections.

ANNUAL REPORT 2024

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, 2024
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. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

The aggregate market value of common stock held by non-affiliates of the registrant computed by reference to the price of the registrant's common stock as of June 28, 2024, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $69.5 million (based on the last reported sale price on the Nasdaq Global Select Market as of such date). As of March 21, 2025, there were 55,900,641 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 2025 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2024. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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References to Spero Therapeutics

Unless otherwise stated, all references to "us," "our," "we," "Spero," "Spero Therapeutics," "the Company" and similar references in this Annual Report on Form 10-K refer to Spero Therapeutics, Inc. and its consolidated subsidiaries. Spero Therapeutics and its associated logos are registered trademarks of Spero Therapeutics, Inc. Other brands, names and trademarks contained in this Annual Report on Form 10-K are the property of their respective owners.

Cautionary Note on Forward-Looking Statements

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:

- our estimates regarding expenses, future revenue and capital requirements and our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash and cash equivalents;
- 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 potential development pathways forward for SPR720;
- the regulatory path forward for tebipenem HBr and the potential approval of tebipenem HBr by the U.S. Food and Drug Administration ("FDA");
- the potential receipt of milestone payments and royalties on future sales under our License Agreement, as amended (the "GSK License Agreement"), with GlaxoSmithKline Intellectual Property (No. 3) Limited ("GSK");
- the potential receipt of milestone payments under our other various license and collaboration agreements;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our ability to secure sufficient capital in the near-term or implement other strategic initiatives to alleviate our current substantial doubt about our ability to continue as a going concern;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the timing and likelihood of regulatory filings and approvals for our product candidates;
- the future development, commercialization, marketing and manufacturing 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 obtain 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;
- the expected benefits and cost-savings from our previously announced strategic restructuring and workforce reduction;
- developments relating to our competitors and our industry;
- the impact of government laws and regulations;
- the impact of general economic conditions, including inflation; 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. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or enter into.

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:

- Our ability to realize the value of tebipenem HBr depends on our commercial partner, GSK, obtaining FDA approval. Even if such approval is obtained, the timeline of, and any requirements imposed as part of, such approval may impact the attractiveness of eventual commercialization of tebipenem HBr through our partnership with GSK.
- Analyses of 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 any of our product candidates 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 or our collaborators 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 any of our product candidates if such product candidates are approved.
- We face substantial competition from other pharmaceutical and biotechnology companies and our operating results may suffer if we fail to compete effectively.
- Pursuant to our previously announced restructuring, we have suspended development of our SPR720 oral program and have shifted our focus and resources to advancing the clinical development of our tebipenem HBr program, as well as other corporate activities. We have also discontinued development of SPR206. Consequently, our business and prospects are substantially dependent on our tebipenem program and our collaboration with GSK. If we fail to execute successfully on this re-prioritized strategic focus, our business and prospects may be materially adversely affected.
- 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 or from our commercial partnership agreements, we could be forced to delay, reduce or eliminate our product development programs.

- We may not achieve the milestones triggering payments to us in our license and collaboration agreements with third parties.
- 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.
- If we fail to comply with our obligations in the agreements under which we in-license or out-license or acquire development or commercialization rights to products, technology or data from or to third parties, we could lose such rights that are important to our business.
- 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 our product candidates, and our ability to generate revenue will be materially impaired.
- The price of our common stock has been and, in the future, may continue to be volatile whether related or unrelated to our operations, which could result in a decline in value for our stockholders.
- Our shares of common stock could be delisted from the Nasdaq GS, which could result in, among other things, a decline in the price of our common stock and less liquidity for holders of shares of our common stock.
- We received a “Wells Notice” from the SEC contemplating a civil enforcement action, which could have a material adverse effect on our business, financial condition and results of operations, prospects, and/or our stock price.

PART I

Item 1. Business.

Overview

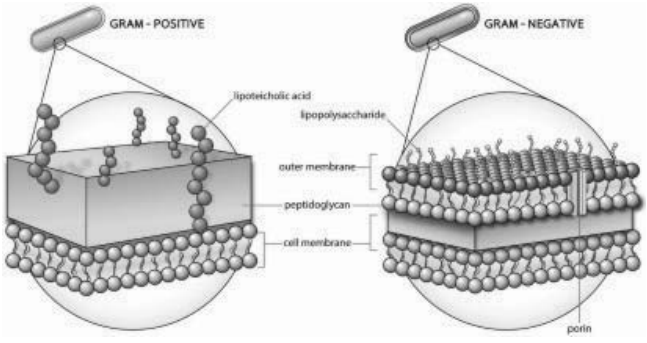
We are a clinical-stage biopharmaceutical company focused on identifying and developing novel treatments for rare diseases and diseases caused by multi-drug resistant ("MDR") bacterial infections with high unmet need. Since our inception in 2013, we have focused our efforts and financial resources on 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 believe that our novel product candidates, if successfully developed and approved, could provide meaningful benefits to patients suffering from serious rare diseases and life-threatening bacterial infections, in both the community and hospital settings. Our pipeline consists of mid- to late-stage clinical assets.

Our most advanced clinical stage product candidate, tebipenem HBr, is in Phase 3 development, with the potential to be the first broad-spectrum oral carbapenem to treat adult patients with complicated urinary tract infections ("cUTIs"), including pyelonephritis, caused by certain microorganisms. The other programs in our pipeline are SPR206 and SPR720. SPR206 is an intravenously ("IV") administered next generation polymyxin product candidate, for the treatment of hospital-acquired and ventilator-associated bacterial pneumonia ("HABP/VABP") caused by MDR Gram-negative bacterial infections. In March 2025, following a reprioritization of our programs, we announced that we are no longer pursuing a planned Phase 2 clinical trial for SPR206. SPR720 is a product candidate for first-line treatment of nontuberculous mycobacterial ("NTM") pulmonary disease. In October 2024, we announced that results from a planned interim analysis of our Phase 2a clinical trial for SPR720 demonstrated the oral agent did not meet its primary endpoint, and we elected to suspend development of SPR720 in its oral formulation. We are currently completing analysis of remaining data from all 25 patients dosed in the trial ahead of determining next steps.

Antibiotic Background

Antibiotics are a class of medications used to treat diseases caused by bacterial infections.

There are two main groups of bacteria, Gram-positive bacteria and Gram-negative bacteria, which are distinguished by structural differences in their cellular envelope. Gram-positive bacteria are surrounded by a single lipid-based cell 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 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 a limited number of bacteria are considered to be narrow-spectrum.
- ***Potency***. Potency refers to the amount of antibiotic required to kill or inhibit growth of bacteria *in vitro*. Potency is commonly expressed as the minimum inhibitory concentration ("MIC") in µg/mL or mg/L, which is the lowest concentration of drug needed to inhibit bacterial growth. 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

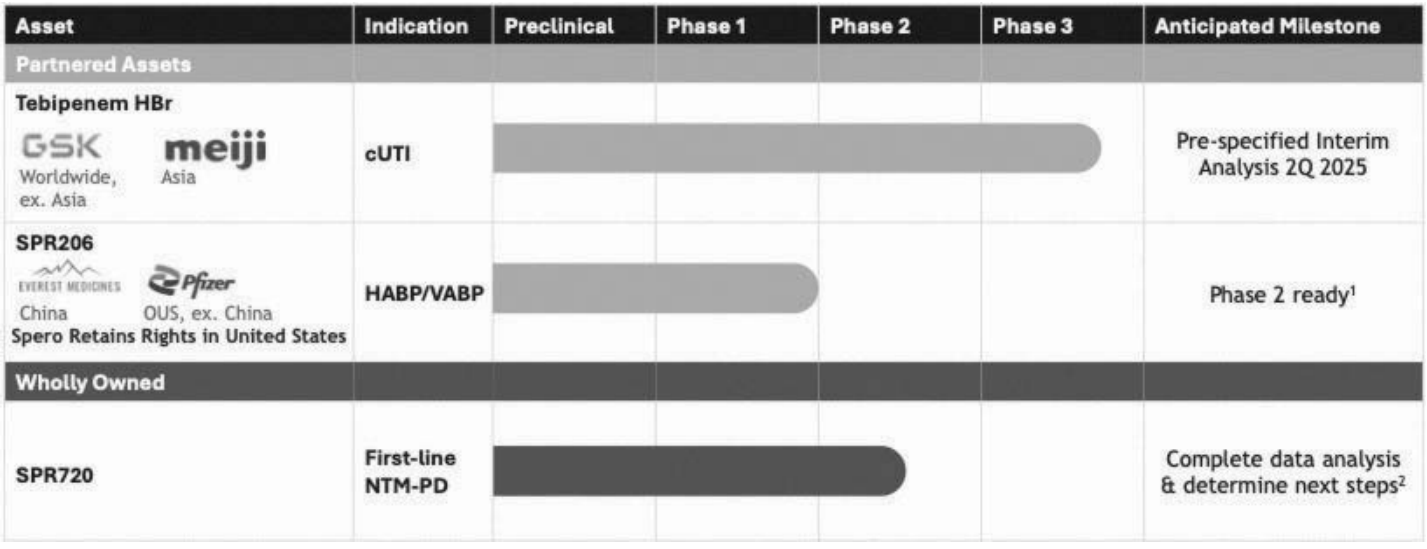
Antibiotic resistance poses a grave threat to global health as resistance rates among various bacteria are increasing. In a systematic analysis examining the global burden of bacterial resistance published in The Lancet, there were an estimated 4.71 million deaths associated with drug-resistant infections in 2021. The Centers for Disease Control and Prevention ("CDC") estimates that the annual impact of antibiotic-resistant infections on the U.S. economy is $20–$35 billion in direct health care costs.

Both Gram-positive and Gram-negative pathogens harbor resistance mechanisms and contribute to the global threat. According to the CDC, Gram-negative pathogens are particularly worrisome because they are increasingly developing resistance to currently used drugs. In 2019, the CDC designated antibiotic-resistant Gram-negative bacteria such as carbapenem-resistant *Acinetobacter baumannii* ("CRAB"), MDR *Pseudomonas aeruginosa* ("MDR PA"), carbapenem-resistant Enterobacterales ("CRE"), and extended-spectrum-β-lactamase ("ESBL")-producing Enterobacterales as urgent or serious threats. These pathogens are associated with significant mortality because of the increased incidence of antibiotic resistance and the lack of effective treatment options. One reason these ESBL -producing pathogens are deemed a serious threat is their ability to spread within the community. This, and their ability to break down commonly used antibiotics, such as penicillins and cephalosporins, make treating cUTI infections more challenging.

As a second example, NTM pulmonary infection that occurs through inhalation of mycobacteria from environmental sources, especially in water and soil, may cause a chronic and progressive pulmonary disease. The estimated total NTM pulmonary disease prevalence in the United States, Europe and Japan is approximately 245,000 diagnosed patients, with approximately 95,000 of these diagnosed patients in the United States. NTM pulmonary disease has a higher frequency among older individuals, particularly women. Most NTM pulmonary disease is due to *Mycobacterium avium* complex ("MAC"), followed by *Mycobacterium abscessus* and *Mycobacterium kansasii*.

Our Clinical Programs

The table below summarizes our anticipated development plans for our product candidates:



1. The Company discontinued the SPR206 program in March 2025
2. The Company has elected to suspend its current development program for the oral dosing of SPR720, as it completes Phase 2a data analysis

Tebipenem HBr (tebipenem pivoxil hydrobromide): Potential First Oral Carbapenem for Use in Adults with cUTI

Disease Overview

Tebipenem HBr is an oral carbapenem in development to treat cUTI, including pyelonephritis, caused by certain microorganisms, in adult patients who have limited oral treatment options.

Urinary tract infections ("UTIs") are among the most common bacterial diseases worldwide and have significant clinical and economic burden. cUTIs are UTIs that are associated with the presence of any number of underlying factors in patients, such as anatomical or functional abnormalities of the urinary tract. Patients with cUTI have a higher risk of recurrence and progression to severe infection, a higher likelihood of harboring a resistant pathogen, and a greater risk of morbidity and mortality, when compared to uncomplicated UTIs.

Limitations of Current Therapies

Currently, fluoroquinolones are the most widely used antibiotic class in treating community and hospital-acquired Gram-negative infections, including UTIs; however, they have encountered increasing resistance among MDR Gram-negative bacteria and are associated with significant adverse effects. Co-resistance further compounds the issue of antibiotic resistance. For instance, more than 40% of *E. coli* isolates with trimethoprim/sulfamethoxazole resistance were co-resistant to levofloxacin.

While current UTI treatment guidelines published by the Infectious Diseases Society of America identify fluoroquinolones as an appropriate empirical therapy option, this recommendation is contingent on local resistance rates being less than 10%. However, the high rates of fluoroquinolone-resistant Escherichia coli ("E. coli") found in the United States today in the community and hospital settings, as shown in the table below, would suggest that there is a need for an antibiotic that is effective against fluoroquinolone-resistant infections.

The table below reflects resistance rates in the United States in the community and hospital settings.

cUTIs in the United States	2024 *E. coli* Resistance Rates to Fluoroquinolones	2019-2022 *E. coli* Resistance Rates to Fluoroquinolones	2013-2014 *E. coli* Resistance Rates to Fluoroquinolones	2000-2004 *E. coli* Resistance Rates to Fluoroquinolones
Community Setting	21.6%	21.5%	11.7%	0%
Hospital Setting	44.3%	37.9%	34.5%	3.5%

In addition, the FDA has issued several warnings against the use of fluoroquinolones in certain patients and determined that fluoroquinolones should be reserved for use in patients with these conditions who have no alternative treatment options; safety warnings in the labeling of fluoroquinolone class products have been further strengthened over the past several years.

Tebipenem HBr Key Attributes

Tebipenem HBr is designed to be the first broad-spectrum oral carbapenem-class antibiotic to treat cUTI, including pyelonephritis caused by certain microorganisms in adults who have limited oral treatment options. Unlike other carbapenems on the U.S. market, 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 the avoidance of IV administration could lead to reduced healthcare resource utilization.

Target Patient Population

We believe tebipenem HBr is well positioned to meet the unmet need for an oral therapy for patients with cUTI, including pyelonephritis, caused by certain microorganisms, who have limited oral treatment options. With an estimated 3.4 million cases each year in the United States, cUTI is a leading cause of infection-related hospitalization. In a nationwide cohort study, the total median 30-day post index all-cause total healthcare costs for cUTI care ranged from $1,531 for patients initially identified in the outpatient setting to $13,028 for patients initially identified in the inpatient setting. While drugs such astrimethoprim/ sulfamethoxazole 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 caused by resistant bacteria, which has led to increased use of IV-administered therapeutics such as carbapenems. Carbapenems have been utilized for more than 30 years and are considered the standard of care for many serious MDR Gram-negative bacterial infections but have only been available as IV-administered formulations. Currently, there are no commercially available oral carbapenems for use in cUTI in adults.

The growing challenges, caused by limited effective oral treatment options for cUTI and pyelonephritis and the increasing resistance rates amongst uropathogens, place a significant burden on both patients and the healthcare system, in terms of recurrent infections, hospitalizations, and cost. Given the observed activity of tebipenem HBr against a broad spectrum of bacterial pathogens, if approved, tebipenem HBr could be used in the hospital setting to transition appropriate patients hospitalized for cUTI to an oral therapy, potentially allowing them to discharge earlier from the hospital.

Tebipenem HBr Clinical Development Overview

GSK License Agreement

In September 2022, we entered into the GSK License Agreement, for the development, manufacturing and commercialization of tebipenem HBr. Pursuant to the GSK License Agreement, we received a $66.0 million upfront payment from GSK with eligibility to receive up to $525.0 million in development, sales, and commercial milestones payments, as well as low single-digit to low double-digit tiered royalties on net product sales. In exchange, GSK received an exclusive license to develop and commercialize tebipenem pivoxil and tebipenem pivoxil HBr in all territories, except Japan, and certain other Asian countries, territories that are retained by our partner Meiji Seika Pharma Co. Ltd. ("Meiji"). Concurrent with the GSK License Agreement, an affiliate of GSK purchased 7,450,000 shares of our common stock at a purchase price of $1.20805 per share for an aggregate purchase price of $9.0 million.

Under the License Agreement, we are responsible for the execution and costs of the follow-up Phase 3 clinical trial of tebipenem HBr. GSK is responsible for the execution and costs of any additional further development, including additional Phase 3 regulatory filing and commercialization activities for tebipenem HBr in the GSK Territory (as defined below). See "Collaboration, License and Service Agreements - Tebipenem HBr Agreements - GSK License Agreement" below for additional information.

Ongoing Clinical Trials

On July 31, 2023, we announced that we received written agreement from the FDA, under a Special Protocol Assessment ("SPA"), on the design and size of PIVOT-PO, a pivotal Phase 3 clinical trial of tebipenem HBr in patients with cUTI, including acute pyelonephritis ("AP").

PIVOT-PO is a global, randomized, double-blind, pivotal Phase 3 clinical trial of oral tebipenem HBr vs. IV imipenem cilastatin, in hospitalized adult patients with cUTI/AP. Patients will be randomized 1:1 to receive tebipenem HBr (600 mg) orally every six hours, or imipenem cilastatin (500 mg) IV every six hours, for a total of seven to ten days. The primary efficacy endpoint will be overall response (composite of clinical cure plus microbiological eradication) at the test-of-cure visit. The primary analysis for the trial will be an assessment of non-inferiority ("NI") in the microbiological intention-to-treat population, based on a 10% NI margin. Randomization is stratified by age, baseline diagnosis (cUTI or AP), and the presence or absence of urinary tract instrumentation.

In December 2023, we commenced enrollment in PIVOT-PO. The pre-planned interim analysis of PIVOT-PO is expected to be completed in the second quarter of 2025.

Completed Clinical Trials

In September 2020, results from the ADAPT-PO Phase 3 clinical trial were announced, comparing the oral regimen of tebipenem HBr with the IV regimen of ertapenem for treating adults with cUTI, including AP. The global, randomized, placebo-controlled clinical trial evaluated safety and efficacy in hospitalized patients, with the primary endpoint being overall response (clinical cure and microbiological response) at the test-of-cure ("TOC") in the microbiological intent-to-treat population.

FDA Status

We included data from our completed ADAPT-PO Phase 3 clinical trial of tebipenem HBr, together with requisite safety data, chemistry, manufacturing and controls ("CMC") information, clinical pharmacology and nonclinical studies, in our New Drug Application ("NDA") submission to the FDA, which was accepted by the FDA in late December 2022. The NDA was seeking approval for tebipenem HBr oral tablets for treatment of cUTI, including pyelonephritis, caused by certain microorganisms in adult patients who have limited oral treatment options. The FDA granted Priority Review designation with a PDUFA target action date of June 27, 2022.

Based upon feedback from an FDA Late Cycle Meeting in late April 2022, we determined to discontinue our own near-term commercialization activities for tebipenem HBr and to restructure our business, including focusing on potential partnership or other opportunities for tebipenem HBr.

In June 2022, we received a Complete Response Letter ("CRL") from the FDA regarding our NDA. In the CRL, the FDA communicated that it had completed its review of the NDA and determined that the NDA could not be approved in its present form. The FDA ultimately concluded that the Phase 3 cUTI clinical trial of tebipenem HBr (ADAPT-PO) was insufficient to support approval and that an additional clinical study would be required to address the deficiency noted in the CRL.

On August 2, 2022, we held a Type A meeting with the FDA to gain further insights as to the pathway forward towards a potential regulatory approval for tebipenem HBr. We also achieved alignment with the FDA on key components of the proposed pivotal Phase 3 trial design. We engaged with the FDA by means of a SPA in the first half of 2023. On July 31, 2023, we announced that we received written agreement from the FDA, under a SPA, on the design and size of the PIVOT-PO clinical trial.

Regulatory Designations

The FDA has designated tebipenem HBr as a Qualified Infectious Disease Product ("QIDP") for the treatment of cUTI, Community-acquired pneumonia ("CABP") and diabetic foot infections ("DFI") under the Generating Antibiotic Incentives Now ("GAIN") Act. Among other benefits of a QIDP designation, the first marketing application for the QIDP-designated indication 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. Additionally, FDA has granted fast track designation for tebipenem HBr in the treatment of cUTI/AP.

SPR206: IV-Administered Investigational Phase 2 Product Candidate Deisgined to Treat MDR Gram-Negative Bacterial Infections in the Hospital Setting.

Disease Overview

MDR and extensively drug-resistant ("XDR") Gram-negative pathogens, including CRAB, MDR PA, and CRE have been classified by the CDC and World Health Organization ("WHO") as serious or urgent/critical threats (CDC 2019, WHO 2017). Currently, the standard-of-care ("SOC") treatment for such infections are associated with low clinical cure rates, stubbornly high mortality rates, and on-therapy resistance development. Fortunately, resistance rates among MDR and CR strains of A. baumannii and P. aeruginosa to the available polymyxin therapeutics including polymyxin B ("PMB") or colistin ("COL") remain relatively low and, consequently, these agents are increasingly being utilized in the treatment of such infections. However, conventional polymyxins are often nephrotoxic and/or neurotoxic. The rise of these resistant pathogens has created an urgent need for novel, safer, and more effective treatment options.

Limitations of Current Therapies

Current SOC therapies for MDR and XDR infections face several limitations, making treatment increasingly challenging. Conventional antibiotics, including carbapenems, cephalosporins, and aminoglycosides, are often ineffective due to widespread resistance mechanisms such as beta-lactamase, efflux pumps, and porin mutations. COL and PMB are among the last-resort options but are associated with significant nephrotoxicity and neurotoxicity, limiting their use. Newer beta-lactam/beta-lactamase inhibitor combinations, while promising, may not cover all resistant strains, particularly metallo-b-lactamase-producing organisms. Additionally, the development of resistance to recently introduced agents raises concerns about the durability of these treatments as monotherapies.

SPR206 Key Attributes

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

- ***Potential to Expand the Potency of SOC 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.

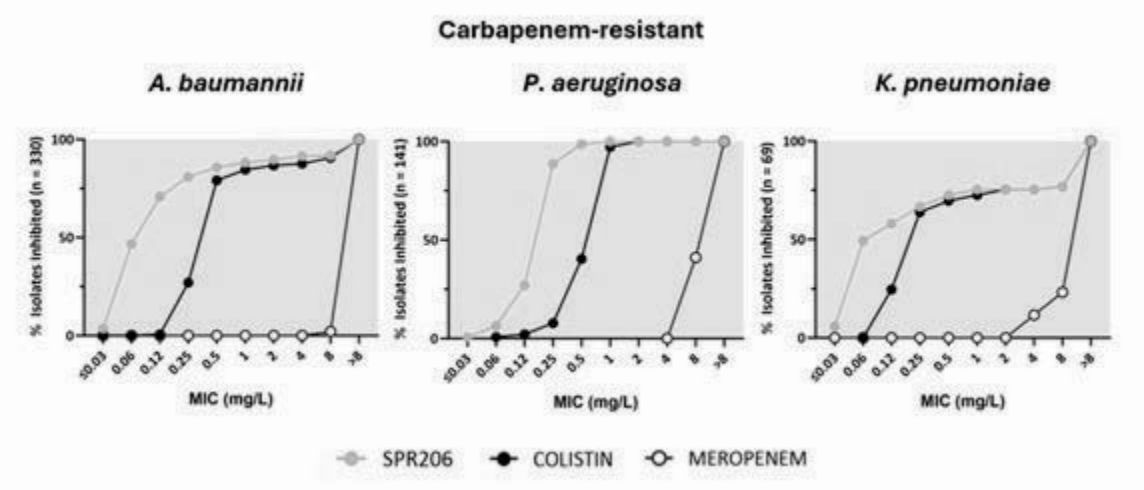
- ***SPR206 Appears to be a Generally Safe and Potent IV-Administered Direct-Acting Agent, Based on Current Data***. SPR206 is designed to interact with lipopolysaccharide ("LPS") to disrupt the outer membrane including that of carbapenem-resistant *P. aeruginosa* and *A. baumannii*. Data from SPR206 *in vitro* and *in vivo* Good Laboratory Practice ("GLP") safety pharmacology and absorption, distribution, metabolism, and excretion ("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 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.
- ***SPR206 is an Investigational Phase 2 Product Candidate***. SPR206 was developed as a treatment for high-risk patients with suspected or known Gram-negative infections such as CRE, CRAB and MDR PA to prevent mortality and reduce the length of stay in the hospital setting. In March 2025, following a reprioritization of our programs, we announced that we are no longer pursuing a planned Phase 2 clinical trial for this program.

Target Patient Population

SPR206 is an investigational Phase 2 product designed to treat hospital-acquired and ventilator-associated bacterial pneumonia only (HABP/VABP) caused by carbapenem-resistant pathogens, infections affecting approximately 25,000 patients in the United States. This next generation polymyxin is well-tolerated and less nephrotoxic compared to Polymyxin B and Colistin according to data currently available. SPR206 exhibits potent antibacterial activity against four major pathogens identified by the CDC as being particularly challenging and enhances the efficacy of SOC agents by increasing kill rates and preventing resistance development. Both preclinical and clinical data support its potential efficacy, lung penetration, and safety/tolerability. Additionally, SPR206 benefits from strong intellectual property protection, with a composition of matter patent valid through 2039, as well as QIDP and fast track designations.

In Vitro Activity of SPR206 against Carbapenem-Resistant Gram-Negative Bacteria

Results from multiple susceptibility studies against contemporary clinical isolates suggest that SPR206 possesses potent activity against CRAB, carbapenem-resistant *P. aeruginosa* and carbapenem-resistant *K. pneumoniae.*



SPR206 Clinical Development Overview

Phase 2 Clinical Trial Update

In February 2024, we announced clearance by the FDA for our IND to evaluate SPR206 in a Phase 2 clinical trial. The Phase 2 clinical trial was designed as a randomized, double-blinded, controlled, multicenter study to evaluate the safety, tolerability, efficacy, and pharmacokinetics ("PK") of SPR206 in combination with select antibiotics for the treatment of patients diagnosed with hospital-acquired and ventilator-associated bacterial pneumonia ("HABP/VABP"), caused by carbapenem-resistant *Pseudomonas aeruginosa*. Approximately 60 adult hospitalized patients were expected to be enrolled. Patients would have received treatment for 7−14 days and evaluated through assessment of post-baseline clinical outcomes.

A Phase 2 clinical trial was supported by preclinical data as well as the results of multiple Phase 1 clinical trials. These Phase 1 trials have demonstrated SPR206's lack of nephrotoxicity at predicted therapeutic dose levels and its ability to achieve mean lung epithelial lining fluid ("ELF") exposures above the MIC for targeted Gram-negative pathogens, when administered three times daily at 100 mg. In March 2025, following a reprioritization of our programs, we announced that we are no longer pursuing a Phase 2 clinical trial for this program.

Completed Clinical Trials

In February 2022, we reported results from a Phase 1 BAL clinical trial designed as an open-label study that enrolled thirty healthy volunteers into five cohorts. The objectives of the study were to evaluate the intrapulmonary PK, including ELF and alveolar macrophage ("AM") concentrations of SPR206 compared to plasma concentrations. These data are important to establish dose requirements for clinical efficacy of SPR206 in the setting of hospital-acquired pneumonia ("HAP")/ventilator-associated pneumonia ("VAP").

Subjects received three 100 mg doses of SPR206 infused every eight hours over one day. Results from the trial showed that SPR206 was generally well-tolerated with a mean lung ELF to plasma concentration ratio of 0.264, with AUC from 0-8 hours used to estimate the total uptake of SPR206. Importantly, the mean concentration of SPR206 in the lung ELF exceeded the SPR206 MIC for targeted gram-negative pathogens for the entirety of the 8-hour dosing period. This study was conducted in collaboration with, and with financial support from, the Department of Defense ("DoD") (Award No. W81XWH1910295). The initiation of this clinical trial triggered the first of two milestone payments related to the study from our development partner, Everest Medicines II Limited ("Everest").

In March 2022, we reported results from the Phase 1 RIS clinical trial, an open-label study that enrolled forty volunteers into five cohorts. Cohort 1 was healthy volunteers, cohorts 2-4 were clinically stable subjects with various degrees of renal impairment, and cohort 5 was clinically stable subjects with end stage renal disease ("ESRD") on hemodialysis. The objectives of the study were to evaluate the PK of SPR206 in healthy subjects and in those with various degrees of renal impairment, including ESRD. These data are important to establish if the concentrations of SPR206 are impacted by differences in renal function and whether dose adjustments for SPR206 would be recommended in such context. Subjects received a single 100 mg infusion of SPR206. Mostly mild but no serious treatment-related adverse events were reported. Systemic exposure to SPR206 increased as renal function decreased, with mean area under the concentration-time curve from time 0 to the last quantifiable concentration (AUC0–last) values 39% to 239% greater in subjects with RI vs healthy subjects. Dose adjustments for patients with renal impairment have been incorporated into the Phase 2 protocol.

The objectives of the study were to evaluate the PK of SPR206 in healthy subjects and in those with various degrees of renal impairment, including ESRD. These data are important to establish if the concentrations of SPR206 are impacted by differences in renal function and whether dose adjustments for SPR206 would be recommended in such context. This study was also conducted in collaboration with, and with financial support from, the DoD (Award No. W81XWH1910295).

Regulatory Designations

SPR206 has been granted QIDP designation and fast track designation by the FDA for the treatment of cUTI and hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP). SPR206 has been granted fast track designation by the FDA for the treatment of HABP and VABP due to carbapenem-resistant *Acinetobacter baumannii-calcoaceticus* complex (CRABc) and carbapenem-resistant *Pseudomonas aeruginosa* (CRPA).

SPR720: Novel Oral Antibiotic for First-Line Treatment of NTM Pulmonary Disease

Disease Overview

NTM-PD is a chronic lung infection caused by a ubiquitous environmental organism that causes pulmonary disease, progressive lung damage and respiratory failure. Patients at risk include those with compromised immune systems or underlying pulmonary disorders. NTM pulmonary disease is associated with a five-year all-cause mortality rate of 35% and high healthcare costs. NTM infections represent a growing global health concern and major unmet medical need because of the lack of new medications to combat these bacteria. MAC is the most common NTM to cause human infection, making up around 80% of all NTM infections.

Limitations of Current Therapies

The current treatment for NTM pulmonary disease is lengthy and involves combination therapy, often three or more antibiotics. In addition, many patients go undiagnosed and could benefit from additional testing. The most common treatment for NTM infections is prolonged combination therapy (continuing for approximately 12–24 months) with drugs traditionally used for tuberculosis ("TB") that have limited efficacy and poor tolerability. Treatment failure is common and is often due to inability to tolerate the regimen or poor adherence.

SPR720 Key Attributes

- ***Novel mechanism.*** SPR720 employs a novel mechanism with no evidence of cross-resistance with marketed antibiotics and low propensity for selection of resistance. Drug resistance to currently available treatments in NTM species threatens adequate control of the disease. A novel mechanism may help evade existing modes of resistance. SPR720 is applicable to both non-refractory and refractory disease.
- ***Broad spectrum of activity.*** SPR720 has demonstrated a broad spectrum of activity in preclinical studies against the most common organisms causing NTM infections, including MAC, *Mycobacterium abscessus* and *Mycobacterium kansasii*.
- ***SPR720 Development Suspended***. In October 2024, we suspended development of the SPR720 oral program for the treatment of NTM-PD, following a planned interim analysis of the Phase 2a proof-of-concept study of SPR720, which demonstrated the study did not meet its primary endpoint. Spero is completing analysis of remaining data from all 25 patients dosed in the trial ahead of determining next steps.

Target Patient Population

NTM infection occurs in many different types of patients. NTM pulmonary disease often occurs in people with compromised immune systems or those with respiratory conditions such as bronchiectasis, chronic obstructive pulmonary disease, cystic fibrosis and asthma. Increasing prevalence of NTM pulmonary disease in the United States is estimated at 6%–10% annually. The estimated total NTM pulmonary disease prevalence in the United States, Europe and Japan is approximately 245,000 diagnosed patients. Women and people aged 65 years or older (a population that is growing in number) have higher incidence and prevalence rates. We believe there is a need for new, potent therapies for NTM pulmonary disease.

SPR720 Clinical Development Overview

Clinical Trials

On November 14, 2022, we announced the re-initiation of a Phase 2a clinical trial of SPR720 (SPR720-202) and that we opened clinical trial sites. The trial enrolled 25 treatment-naïve or treatment-experienced, non-refractory patients with NTM pulmonary disease, due to MAC. The primary endpoint of the study was evaluating changes in bacterial load in sputum samples from baseline to the end of the 56-day treatment period. Key secondary endpoints include assessments of clinical response, PK, safety and tolerability and quality of life. Trial enrollment concluded in July 2024.

Additionally, we conducted two Phase 1 clinical trials – one to assess intrapulmonary PK of SPR719 (the active moiety of the prodrug SPR720) in a bronchoalveolar lavage ("BAL") study and another to evaluate the effect on the PK of SPR720, azithromycin and ethambutol when co-administered together in healthy volunteers.

In October 2024, we suspended development of the SPR720 oral program for the treatment of NTM-PD, following a planned interim analysis of the Phase 2a proof-of-concept study of SPR720, which demonstrated the study did not meet its primary endpoint. While data showed antimicrobial activity associated with SPR720, the analysis did not show sufficient separation from placebo and highlighted potential dose limiting safety issues in patients dosed at 1,000 mg orally once daily, including three cases of reversible grade 3 hepatotoxicity. We are completing analysis of the remaining data from all 25 patients dosed in the trial ahead of determining next steps.

Regulatory Designations

The FDA has granted orphan drug designation to SPR720 for the treatment of nontuberculous mycobacteria infection, 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. We received QIDP designation by the FDA for SPR720 for the treatment of lung infections caused by nontuberculous mycobacteria and for the treatment of lung infections caused by *M. tuberculosis*. In addition, SPR720 also was awarded fast track designation by the FDA for treatment of adult patients with NTM pulmonary disease. Neither the QIDP nor orphan drug designation nor fast track designation, however, guarantee a faster development process or ensure FDA approval.

Our Strategy

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

- ***In partnership with GSK, advance tebipenem HBr through completion of the Phase 3 clinical trial and advise and consult with GSK through the regulatory approval process.*** We granted GSK an exclusive license to develop and commercialize tebipenem pivoxil and tebipenem pivoxil HBr in all territories, except Japan, and certain other Asian countries, territories which are retained by our partner Meiji. We are responsible for execution and costs of the tebipenem HBr Phase 3 clinical trial in the United States. GSK is responsible for the execution and costs of regulatory and commercial activities for tebipenem HBr in the United States, as well as territories outside of the United States (not including the Meiji Territory (as defined below)).
- ***Selectively expand our portfolio of product candidates to develop therapies to address high unmet need in addressable patient populations, including those diagnosed with rare and infectious diseases.*** We are using our expertise to actively build and expand a portfolio of product candidates for the treatment of rare diseases and infections where unmet need exists. In addition, we are leveraging our deep-rooted relationships in the academic, medical and corporate communities to identify and develop new and innovative therapies in other tangential disease areas. Assessing our product candidates relies on three principles: 1) unmet medical need, 2) novel mechanism or formulation differentiation to overcome challenges with current therapeutics, and 3) convenience for patients.
- ***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.
- ***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 ("NIAID"), the DoD and the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator ("CARB-X") a public-private partnership funded by BARDA within the United States Department of Health and Human Services. We intend to continue to pursue collaborations with government agencies and non-profit foundations, to the extent available and practicable, to support the development of our product candidates.

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 license agreements (described below) pursuant to which we have granted certain development, manufacturing and commercialization rights with respect to certain of our product candidates.

Tebipenem HBr Agreements

GSK License Agreement

On November 7, 2022, we closed the transactions contemplated by the GSK License Agreement, which was entered into on September 21, 2022. Pursuant to the terms of the GSK License Agreement, we granted GSK an exclusive royalty-bearing license, with the right to grant sublicenses, under our intellectual property and regulatory documents and a sublicense under certain intellectual property of Meiji and Meiji's regulatory documents to develop, manufacture and commercialize tebipenem pivoxil and tebipenem HBr and products that contain tebipenem pivoxil and tebipenem HBr (the "GSK Licensed Products") in all territories, except certain Asian countries previously licensed to Meiji (Japan, Bangladesh, Brunei, Cambodia, China, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, South Korea, Taiwan, Thailand and Vietnam (collectively, the "Meiji Territory")) (the "GSK Territory"). If our license with Meiji is terminated, or if Meiji forfeits or loses its rights to develop, manufacture and commercialize tebipenem HBr and products that contain tebipenem HBr in any countries in the Meiji Territory, then GSK will have an exclusive first right to negotiate with us to add any such countries to the GSK Territory.

Under the terms of the GSK License Agreement, we received an upfront payment of $66.0 million for GSK to secure rights to the medicine, and GSK also invested $9.0 million in our common stock.

In July 2023, we received written agreement from the FDA, under a SPA, on the design and size of PIVOT-PO, a pivotal Phase 3 clinical trial of tebipenem HBr in patients with cUTI, including AP. Under the terms of the GSK License Agreement, we received a $30.0 million development milestone payment during the third quarter of 2023.

In December 2023, we commenced enrollment in PIVOT-PO with its first patient, first visit. Under the terms of the GSK License Agreement, we are entitled to receive a $95.0 million development milestone that is payable in four equal semiannual installments. We received the first installment payment of $23.8 million for such development milestone in February 2024, the second installment payment of $23.8 million in August 2024 and the third installment payment of $23.8 million in February 2025. The final installment payment of $23.8 million is expected to be received in the third quarter of 2025.

Remaining potential payments under the GSK License Agreement are milestone and royalty based, and are as follows (in millions):

Event	Milestone payments (up to)
GSK's submission of a NDA with the FDA for tebipenem HBr	$25.0
Total commercial milestone payments based on first sale (US/EU)	$150.0
Total potential sales milestone payments	$225.0
Royalties	Low-single digit to low-double digit (if sales exceed $1.0 billion) tiered royalties on net product sales

Amendments to the GSK License Agreement

In July 2023, we entered into Amendment 1 to the GSK License Agreement, which updated the timeframe for technology transfer in the GSK License Agreement.

In December 2023, we entered into Amendment 2 to the GSK License Agreement, which added a country to the locations for PIVOT-PO enrollment. Under the terms of Amendment 2 we are entitled to an additional $4.3 million in milestones based on activities in such country. We received the first milestone payment of $1.2 million in August 2024 and received the second milestone payment of $1.3 million in October 2024. The third milestone of $0.7 million was achieved in December 2024 and payment was received in February 2025.

In March 2024, we entered into Amendment 3 to the GSK License Agreement, which assigns our rights to Product Trademarks (as defined in Amendment 3) to GSK.

In October 2024, we entered into Amendment 4 to the GSK License Agreement, under which we will receive an additional $0.8 million upon completion of activities related to an additional Phase 1 clinical study. We received $0.4 million of the milestone in January 2025 and anticipate receipt of the outstanding balance in the second quarter of 2025.

Royalties are subject to reduction in the event of third-party licenses, entry of a generic product or expiration of patent and regulatory exclusivity prior to the tenth anniversary of the first commercial sale of a GSK Licensed Product in a particular country.

We are responsible for the execution and costs of the Phase 3 clinical trial of tebipenem HBr. GSK is responsible for the execution and costs of any additional further development, including additional Phase 3 trials, regulatory filings and commercialization activities for tebipenem HBr in the GSK Territory. We will also be responsible for providing and paying for the clinical supply of tebipenem HBr while GSK will be responsible for the costs of the commercial supply of tebipenem HBr. A joint development committee has been established between GSK and us to coordinate and review development activities for tebipenem HBr in the United States.

Unless earlier terminated due to certain material breaches of the GSK License Agreement or by GSK for convenience, or otherwise, the GSK License Agreement will expire on a jurisdiction-by-jurisdiction and GSK Licensed Product-by-GSK Licensed Product basis on the latest to occur of (i) loss of patent exclusivity, (ii) loss of regulatory exclusivity or (iii) ten years following the date of the first commercial sale of such licensed product in such country (the “GSK Royalty Term”). During the GSK Royalty Term, we have agreed not to develop, manufacture or commercialize any oral carbapenem for any indication or any oral antibiotic for cUTI; this restriction does not apply to any third party which acquires control of us after the date of the GSK License Agreement if certain conditions are met.

We have the right to terminate the GSK License Agreement upon a material breach by, or bankruptcy of, GSK. GSK has the right to terminate the GSK License Agreement at any time upon a specified number of days’ notice or upon a material breach by, or bankruptcy of, us. In addition, in the event that GSK has the right to terminate the GSK License Agreement due to a material breach by us, GSK may elect not to terminate the GSK License Agreement and in lieu thereof may assume the responsibility and expense of development of tebipenem HBr in the United States, in which event GSK’s obligation to make further development payments to us

(including unpaid installments of any earned milestone payments) would cease, and/or to reduce all subsequent commercial and sales milestone payments and royalty payments otherwise due by GSK to us under the GSK License Agreement by 50%. In the case of a Change of Control of Spero, GSK similarly may, in lieu of terminating the GSK License Agreement, assume responsibility and expense of development of tebipenem HBr in the United States and no development milestones would be payable to Spero, as described above.

The GSK License Agreement contains representations and warranties, other covenants, indemnification provisions and other terms and conditions customary for transactions of the type contemplated by the GSK License Agreement. In support of certain of its rights to indemnification, GSK also has certain rights to suspend payments otherwise owed to us, as well as the right to offset payments otherwise owed to the Company against certain indemnifiable claims.

Meiji Agreements

To support our development of tebipenem HBr, in June 2017 we entered into an exclusive License Agreement with Meiji (the "Meiji License"). Pursuant to the Meiji License, we obtained know-how, data and regulatory documents that have supported the development of tebipenem HBr and which we believe will help support the regulatory approval of tebipenem HBr.

We and our collaboration partners, including GSK, retain exclusive rights to commercialize tebipenem HBr throughout the world, except in the Meiji Territory, 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 have established a joint commercialization committee to coordinate information sharing relative to the commercialization of tebipenem HBr.

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 a global pharmaceutical company, to which we refer as 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 non-refundable upfront fee of $0.6 million, a $1.0 million milestone payment to Meiji upon the enrollment of the first patient in our Phase 1 clinical trial of tebipenem HBr in October 2017 and a $1.0 million milestone payment upon submission of the NDA for tebipenem HBr in October 2021. We are obligated to pay Meiji future clinical and regulatory milestone payments up to an aggregate of $1.0 million and royalties of a low single-digit percentage based on net sales of tebipenem HBr. Additionally, we were obligated to pay Meiji a percentage of certain amounts received from any sublicensees, up to an aggregate of $7.5 million; which we fully satisfied in the fourth quarter of 2023. We recorded these amounts as research and development expenses in our consolidated statement of operations.

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 did not contemplate us having any right to sublicense the Global Pharma know-how. Prior to our entering into the GSK License Agreement, in February 2022, Meiji received written approval from Global Pharma permitting Meiji to provide us the right to sublicense the Global Pharma know-how.

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.

SPR206 Agreements

Cantab Agreements

In June 2016, we entered into a stock purchase agreement (the "Cantab Agreement") with Pro Bono Bio PLC, a corporation organized under the laws of England, and its affiliates, including PBB Distributions Limited ("PBB"), Cantab Anti-Infectives Ltd. ("CAI") and New Pharma License Holdings Limited ("NPLH"). This agreement allows us to acquire NPLH and its intellectual property rights and assets relating to our polymyxin products, and our next-generation potentiating agents in particular. The intellectual property portfolio we acquired includes patents that 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 ($6.3 million as of December 31, 2024) 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 equity interest in Spero Cantab and entered into a subscription agreement and stockholders agreement with PBB. In July 2017, we repurchased PBB's minority equity interest in Spero

Cantab in exchange for a one-time non-refundable 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.

Everest Medicines License Agreement

On January 4, 2019, we, through NPLH, entered into a license agreement (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. 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 ("Everest 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 "Everest Territory." We retained development, manufacturing and commercialization rights with respect to SPR206 and Everest Licensed Products in the rest of the world and also retained the right to develop or manufacture SPR206 and Everest Licensed Products in the Everest Territory for use outside the Everest 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 Everest 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.

On January 15, 2021, we entered into an amended and restated license agreement (the "Amended Everest License Agreement") with Everest and Spero Potentiator, Inc., 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 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, we assigned patents in the Everest 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, we are also entitled to receive high single-digit to low double-digit royalties on net sales, if any, of Everest Licensed Products in the Everest Territory following regulatory approval of SPR206. Everest has the right to sublicense to affiliates and third parties in the Everest Territory.

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

Pfizer License and Share Purchase Agreements

On June 30, 2021, we entered into a License Agreement (the "Pfizer License Agreement") and a Share Purchase Agreement (the "Pfizer Purchase Agreement") with Pfizer, Inc. ("Pfizer"). Under the terms of the Pfizer License Agreement, we granted Pfizer an exclusive royalty-bearing license to develop, manufacture and commercialize SPR206 or products that contain SPR206 (the "Pfizer Licensed Products") globally with some territorial exceptions (the "Pfizer Territory"). The Pfizer Territory excludes the United States and the Asian markets previously licensed to Everest in the Everest Territory.

In connection with the Pfizer Purchase Agreement, Pfizer purchased 2,362,348 shares of our common stock at a price of $16.93 per share for a total investment of $40.0 million. Under the terms of the Pfizer License Agreement, we received no other upfront payments but are eligible to receive up to $80.0 million in development and sales milestones, and we may also receive high single-digit to low double-digit royalties on net sales of SPR206 in the Pfizer Territory. Achievement of these payments cannot be guaranteed. We and Pfizer agree that upon Pfizer's request, the parties will negotiate in good faith regarding procuring a clinical or commercial supply of the compound.

In September 2022, we received a $5.0 million payment from Pfizer in connection with the achievement of a regulatory milestone specified in the Pfizer License Agreement.

We are responsible for all costs related to developing and obtaining regulatory approval of SPR206 and Pfizer Licensed Products in the Pfizer Territory, with a focus on the European market, and are obligated to use commercially reasonable efforts, including to achieve certain specified diligence milestones within agreed-upon periods. A joint development committee was established between Pfizer and us to coordinate and review the development, manufacturing and commercialization plans with respect to Pfizer Licensed Products in the Pfizer Territory. Pfizer is responsible for commercializing SPR206 and the Licensed Products in the Pfizer Territory.

Unless earlier terminated due to certain material breaches of the contract or by Pfizer's convenience, or otherwise, the Pfizer License Agreement will expire on a jurisdiction-by-jurisdiction and licensed product-by-licensed product basis after ten years from the effective date. The Pfizer License Agreement will automatically renew for an additional ten-year term unless terminated.

SPR720 Agreements

Vertex Assignment and License Agreement

In May 2016, we entered into an agreement with Vertex Pharmaceuticals Incorporated ("Vertex") pursuant to which Vertex assigned to us rights to patents relating to the oral prodrug 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 expenses 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 one year.

Government Awards

Through December 31, 2024, we have committed funding support of up to an aggregate of $85.4 million in non-dilutive funding from BARDA, NIAID and concluded awards from CARB-X, SBIR and the DoD, with the potential to receive a total of up to $114.6 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 $72.0 million for qualified expenses for tebipenem HBr development. 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. In December 2023, BARDA extended the period of performance for the first contract option through December 31, 2025 and the contract was modified to include additional funding of $0.6 million for tebipenem HBr, increasing the amount of the first contract option to $16.5 million.

There is a second option exercisable by BARDA for $12.7 million of funding, subject to the achievement of specified milestones under the award agreement and program direction. In January 2022, BARDA added, and exercised, a third option to the original award, increasing the total amount of committed funding by $12.9 million. In September 2022, remaining funding from the $12.9 million option was reprogrammed into a fourth contract option to support clinical trials for patients with cUTI, including AP. In July 2024, an additional contract modification of $11.7 million was executed under our existing contract with BARDA.

As of December 31, 2024 the total amount of committed funding under the BARDA award was $59.3 million of which the Company has cumulatively recognized $56.7 million in grant revenue.

The Defense Threat Reduction Agency ("DTRA") may provide up to $10.0 million in addition to the total potential $72.0 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.

- ***NIAID funding for SPR206.*** In May 2021, a NIAID contract was awarded for SPR206 providing total development funding of up to $23.4 million, of which $7.1 million has been committed. The award initially committed funding of $2.1 million over a two-year base period from May 2021 to January 2023 for nonclinical, regulatory, and CMC activities. In December 2022, NIAID extended period of performance for the base period until August 16, 2023. In December 2022, the contract was modified to include additional funding of approximately $0.1 million, increasing the amount of base period committed funding to $2.2 million. In October 2022, NIAID exercised its first option under the contract, committing $4.0 million for SPR206 through April 2025. In June 2023, NIAID extended the period of performance for the base period until January 16, 2024 and in August 2023, the contract was modified to include additional funding of approximately $0.1 million increasing the amount of base period committed funding to $2.3 million. In August 2023, NIAID exercised its third option under the contract, committing $0.8 million for SPR206 through August 2024. In December 2023, the period of performance for the base period was extended through September 16, 2024. In August 2024, an additional contract modification of $3.4 million was executed under Option 1 of our existing contract with NIAID for SPR206 Phase 2 start up activities.

As of December 31, 2024, the total amount of committed funding under the NIAID award was $10.5 million and the total potential contract value was $27.0 million. Of the committed funding, the Company has cumulatively recognized $5.3 million in grant revenue.

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 the know-how and continuing technological innovation to develop and maintain our proprietary position.

Spero-Owned Intellectual Property Relating to Compounds Under Development

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

Tebipenem HBr Oral Carbapenem (Tebipenem Pivoxil Hydrobromide)

Our tebipenem HBr program contains one issued and three pending United States patent applications, and 40 issued and 30 pending foreign patent applications covering novel solid forms of tebipenem pivoxil hydrobromide and novel pharmaceutical formulations of tebipenem pivoxil hydrobromide as of December 31, 2024, all wholly owned by us. The issued foreign patents are issued in Australia, Brazil, Canada, the Eurasian Patent Office ("EAPO"), which includes Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Russia, Tajikistan and Turkmenistan, Indonesia, Israel, Japan, Mexico, New Zealand, South Korea, and South Africa. Foreign patent applications are pending in Australia, Brazil, Canada, China, Colombia, the European Patent Office, Egypt, Indonesia, Israel, India, Japan, South Korea, Mexico, New Zealand, the Philippines, Singapore, Thailand, and Vietnam. U.S. and foreign patents covering our tebipenem pivoxil hydrobromide preparations will have statutory expiration dates of December 2037, February 2038, and November 2041. Patent term adjustments or patent term extensions could result in later expiration dates.

In January 2021, the USPTO issued U.S. Patent No, 10,889,587, which is directed to the crystalline formulation of tebipenem HBr, our 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.

NTM Pulmonary Disease Program (SPR720)

Our intellectual property portfolio for our DNA Gyrase Inhibitor program includes issued patents and a pending patent application directed to composition of matter for SPR720, a prodrug of SPR719. The SPR719 and SPR720 patents include patents to close analogs, novel solid forms, methods of manufacture for both compounds, 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, 2024, we owned 11 issued U.S. patents, 98 issued foreign patents, and one pending U.S. application and 8 pending foreign patent applications. The issued foreign patents are in a number of jurisdictions including the European Union and its member states, Argentina, Australia, Brazil, Canada, China, Hong Kong, Indonesia, Israel, India, Japan, South Korea, Mexico, New Zealand, the Philippines, Russia, Singapore, South Africa, and Taiwan. Issued U.S. and foreign patents, and patents issuing from the pending PCT application, will have statutory expiration dates of January 2032, June 2032, July 2033 and October 2042. Patent term adjustments or patent term extensions could result in later expiration dates.

Next-Generation Potentiator Product (SPR206)

The intellectual property portfolio for our next-generation polymyxin program contains patent applications and issued patents directed to a 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, 2024, we owned four U.S. patents and three pending U.S. patent applications, 138 foreign patents, and 21 pending foreign patent applications in a number of jurisdictions including Argentina, Australia, Brazil, Canada, China, Colombia, the European Patent Office, India, Israel, Japan, Mexico, New Zealand, the Philippines, Russia, Singapore, South Africa, Taiwan, Ukraine and Venezuela. Issued U.S. or foreign patents and any patents issued from pending U.S. or foreign applications covering our next-generation polymyxin program will have a statutory expiration date of May 2034, March 2035, November 2035 or June 2039. Patent term adjustments or patent term extensions could result in later expiration dates.

In October 2022, the USPTO issued U.S. Patent No. 11,459,357, which covers the SPR206 composition of matter and formulations thereof, as well as methods of treating a bacterial infection with SPR206. The patent is assigned to us and has a lifespan extending into at least June 2039.

In 2019, we entered into an agreement with Everest, by which Everest would develop, manufacture, and commercialize SPR206 in China, South Korea, and certain Southeast Asian countries. Our agreement with Everest has since been amended to include an obligation by us to assign its SPR206 patent rights to Everest in these countries and assignments to Everest have now been executed.

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.

Russian and Eurasian Patent Office and Ukrainian Patents

Due to the war in Ukraine and sanctions between the United States and Russia, patents and patent applications in Russia, the EAPO and Ukraine currently have an uncertain fate. Further, the Kremlin has stated it will no longer enforce patents held by businesses in "unfriendly" countries, in effect giving a royalty free license to all patents and patent applications filed by United States entities in Russia. Until the conflict with Ukraine ends, our Russian and EAPO patents will not be enforced.

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 the physical security of our premises and the 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 partnered product candidate, tebipenem HBr, if approved, will be efficacy, coverage of drug-resistant strains of bacteria, safety, and tolerability profile, reliability, the convenience of oral dosing, price, availability of reimbursement from governmental and other third-party payers and susceptibility to drug resistance.

In partnership with GSK, we are developing tebipenem HBr as an oral antibiotic for use as a monotherapy for the treatment of resistant and MDR infections. If approved, there are a variety of available oral therapies for the treatment of cUTIs that we expect would compete with tebipenem HBr, such as levofloxacin, ciprofloxacin and trimethoprim/sulfamethoxazole and several antibiotics currently in clinical development for cUTI. 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;
- oral dosing regimen and opportunity to step-down from IV-administered therapy; and
- as a monotherapy treatment for MDR Gram-negative infections.

SPR206 is designed as a treatment for high-risk patients with suspected or known Gram-negative infections, such as CRE, CRAB and MDR PA to prevent mortality and reduce the length of stay in the hospital setting. 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., meropenem-vaborbactam (Vabomere) from Melinta Therapeutics, Inc, cefiderocol (Fetroja) from Shionogi & Co. Ltd., imipenem-relebactam (Recarbrio) from Merck & Co, and sulbactam/durlobactam (Xacduro) from Innoviva Specialty Therapeutic. Each of these products and product candidates employs a mechanism of action that differs from the mechanism of action employed by SPR206.

We have been developing SPR720 as a treatment for NTM pulmonary disease. There are currently no agents approved to treat non-refractory NTM pulmonary disease. Only one drug is currently 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. There are also a number of late-stage product candidates in clinical development by Paratek Pharmaceuticals, Inc., Mannkind Corporation, AN2 Therapeutics, Inc. and Insmed, Inc. that are intended to treat refractory disease and first-line treatment of disease due to MAC or M. absesssus.

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

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

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with 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 ("IRB") before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices ("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 ("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. The Consolidated Appropriations Act for 2023, signed into law on December 29, 2022, (P.L. 117-328), amended the FDCA to specify that nonclinical testing for drugs may, but is not required to, include *in vivo* animal testing. According to the amended language, a sponsor may fulfill nonclinical testing requirements by completing various *in vitro* assays (e.g., cell-based assays, organ chips, or microphysiological systems), *in silico* studies (i.e., computer modeling), other human or non-human biology-based tests (e.g., bioprinting), or *in vivo* animal tests.

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 and human clinical trials have begun. 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 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 ("NIH") for public dissemination on the Clinicaltrials.gov registry. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government. The government has recently begun enforcing these registration and results reporting requirements against non-compliant clinical trial sponsors.

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, ADME and, if possible, to gain an early indication of its effectiveness. During Phase 1 clinical trials, sufficient information about the investigational drug's PK 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.

Congress recently amended the FDCA to require sponsors of a Phase 3 clinical trial, or other "pivotal study" of a new drug to support marketing authorization, and to design and submit a diversity action plan for such clinical trial. The action plan must include the sponsor's diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. Sponsors must submit a diversity action plan to the FDA by the time the sponsor submits the relevant clinical trial protocol to the FDA for review. The FDA may grant a waiver for some or all of the requirements for a diversity action plan. If the FDA objects to a sponsor's diversity action plan or otherwise requires significant changes to be made, it could delay initiation of the relevant clinical trial.

Post-approval trials, sometimes referred to as "Phase 4" clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of Phase 4 clinical trials.

Interactions with FDA During the Clinical Development Program

Following the clearance of an IND and the commencement of clinical trials, the sponsor will continue to have interactions with the FDA. Progress reports detailing the results of clinical trials must be submitted at least annually to the FDA and more frequently if serious AEs occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or potentially animal studies to assess toxicity or in vitro testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the occurrence of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. 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 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.

In addition, sponsors are given opportunities to meet with the FDA at certain points in the clinical development program. Specifically, sponsors may meet with the FDA prior to the submission of an IND (pre-IND meeting), at the end of Phase 2 clinical trial (EOP2 meeting) and before an NDA is submitted (pre-NDA meeting). Meetings at other times may also be requested. There are six types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-NDA meetings, as well as end of phase meetings such as EOP2 meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product, including, for example, meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use. Type D meetings are focused on a narrow set of issues that may be critical to move a program forward, while so-called "INTERACT" meetings are intended for novel products and development programs that present unique challenges in early development.

These meetings provide an opportunity for the sponsor to share information about the data gathered to date with the FDA and for the FDA to provide advice on the next phase of development. For example, at an EOP2, a sponsor may discuss its Phase 2 clinical results and present its plans for the pivotal Phase 3 clinical trial(s) that it believes will support the approval of the new product. Such meetings may be conducted in person face-to-face, virtual face-to-face (video conference), or written response only with minutes reflecting the questions that the sponsor posed to the FDA and the agency's responses. The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. Nonetheless, from a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure.

Acceptance of NDAs

Assuming successful completion of the required clinical testing, the results of the nonclinical studies and clinical trials, along with information relating to the product's chemistry, manufacturing, controls, safety updates, patent information, abuse information and proposed labeling, are submitted to the FDA as part of an application requesting approval to market the product candidate for one or more indications. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of a drug product. The fee required for the submission and review of an application under the Prescription Drug User Fee Act (the "PDUFA"), is substantial (for example, for fiscal year 2025 this application fee is over $4.3 million), and the sponsor of an approved application is also subject to an annual program fee, currently more than $404,000 per eligible prescription product. These fees are typically adjusted annually, and exemptions and waivers may be available under 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. Congress is required to reauthorize the agency's user fee programs every five years, and current legislative provisions supporting the PDUFA program are set to expire on September 30, 2027.

The application review process begins upon receipt of the application. The PDUFA time clock begins on the FDA receipt date except for eligible products (i.e., new molecular entity ("NME") NDAs and original biologics license applications ("BLAs")). For these applications, the PDUFA time clock begins 60 days after the application receipt date if the application is filed; however, the review timeline for all applications begins on the day of submission. The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. In pertinent part, the FDA's regulations state that an application "shall not be considered as filed until all pertinent information and data have been received" by the FDA. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File ("RTF") determination to the applicant. Typically, an RTF will be based on administrative incompleteness, such as clear omission of information or sections of required information; scientific incompleteness, such as omission of critical data, information or analyses needed to evaluate safety and efficacy or provide adequate directions for use; or inadequate content, presentation, or organization of information such that substantive and meaningful review is precluded. The FDA may request additional information rather than accept an application for filing. In this event, the application must be resubmitted with additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

Review of NDAs

After the submission is accepted for filing, the FDA begins an in-depth substantive review of the application. The FDA reviews the application to determine, among other things, whether the proposed product is safe and effective for its intended use, whether it has an acceptable purity profile and whether the product is being manufactured in accordance with cGMP.

Under the current PDUFA goals and policies agreed to by the FDA, the agency has ten months from the filing date in which to complete its initial review of a standard application that is a NME, and six months from the filing date for an NME application with "priority review". The review process may be extended by the FDA for three additional months to consider new information or in the case of a clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission. Despite these review goals, it is not uncommon for FDA review of an application to extend beyond the PDUFA target action date.

In connection with its review of an application, the FDA will typically submit information requests to the applicant and set deadlines for responses thereto. The FDA will also conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether the manufacturing processes and facilities comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications.

The FDA also may inspect the sponsor and one or more clinical trial sites to assure compliance with IND and GCP requirements and the integrity of the clinical data submitted to the FDA. To ensure cGMP and GCP compliance by its employees and third-party contractors, an applicant may incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control. The FDA generally accepts data from foreign clinical trials in support of an NDA if the trials were conducted under an IND. If a foreign clinical trial is not conducted under an IND, the FDA nevertheless may accept the data in support of an NDA if the study was conducted in accordance with GCPs and the FDA is able to validate the data through an on-site inspection, if deemed necessary. Although the FDA generally requests that marketing applications be supported by some data from domestic clinical trials, the FDA may accept foreign data as the sole basis for marketing approval if (1) the foreign data are applicable to the U.S. population and U.S. medical practice, (2) the studies were performed by clinical investigators with recognized competence, and (3) the data may be considered valid without the need for an on-site inspection or, if the FDA considers the inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

Additionally, the FDA may refer an application, including applications for novel product candidates which present difficult questions of safety or efficacy, to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. Typically, 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 recommendation of an advisory committee, but it considers such recommendations when making final decisions on approval.

Data from clinical trials are not always conclusive, and the FDA or its advisory committee may interpret data differently than the sponsor interprets the same data. The FDA may also re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process or delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all.

The FDA also may require submission of a Risk Evaluation and Mitigation Strategy ("REMS") if it determines that a REMS is necessary to ensure that the benefits of the product outweigh its risks and to assure the safe use of the product. The REMS could include medication guides, physician communication plans, assessment plans and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS and the FDA will not approve the application without a REMS.

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.

Decisions on NDAs

The FDA reviews an application to determine, among other things, whether the product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The term "substantial evidence" is defined under the FDCA as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the product involved, on the basis of which it could fairly and responsibly be concluded by such experts that the product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."

The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, the FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. This approach was subsequently endorsed by Congress in 1998 with legislation providing, in pertinent part, that "If [FDA] determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the FDA may consider such data and evidence to constitute substantial evidence." This modification to the law recognized the potential for the FDA to find that one adequate and well controlled clinical investigation with confirmatory evidence, including supportive data outside of a controlled trial, is sufficient to establish effectiveness. In December 2019, the FDA issued draft guidance further explaining the studies that are needed to establish substantial evidence of effectiveness. It subsequently issued a complementary draft guidance on demonstrating substantial evidence of effectiveness based on one adequate and well-controlled clinical investigation plus confirmatory evidence in September 2023. Although neither has been finalized to date, together these two FDA guidance documents provide additional information for industry on the flexibility in the amount and type of evidence needed to establish the effectiveness of new drug products.

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a CRL or an approval letter. To reach this determination, the FDA must determine that the drug is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks. In connection with this assessment, the FDA review team will assemble all individual reviews and other documents into an "action package," which becomes the record for FDA review. The review team then issues a recommendation, and a senior FDA official makes a decision.

A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time- consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the applicant will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the applicant an extension to respond and resubmit. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. The FDA has taken the position that a CRL is not final agency action making the determination subject to judicial review.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (e.g., patient population, indication) described in the FDA-approved labeling. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials 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.

Under the Ensuring Innovation Act, which was signed into law in April 2021, the FDA must publish action packages summarizing its decisions to approve new drugs within 30 days of approval of such products. To date, CRLs are not publicly available documents.

FDA Expedited Review Programs

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 make important new drugs available 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 a 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, including pyelonephritis, caused by certain microorganisms in adult patients who have limited oral treatment options. 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 ("FDASIA") in 2012, Congress created a 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 (the "GAIN Act") which directed the FDA to implement the 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 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 an NME (or an original BLA) 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 ("IMM") and that is reasonably likely to predict an effect on IMM or other clinical benefits, 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 endpoints, 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. In addition, Congress recently provided FDA additional statutory authority to mitigate potential risks to patients from continued marketing of ineffective drugs previously granted accelerated approval. Under these recent amendments to the FDCA, the agency may require a sponsor of a product granted accelerated approval to have a confirmatory trial underway prior to approval. The sponsor must also submit progress reports on a confirmatory trial every six months until the trial is complete, and such reports will be published on the FDA's website. 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. Lawmakers, FDA officials, and other stakeholders have recently been evaluating the accelerated approval program and have proposed potential reforms to improve certain aspects and in February 2024 the FDA announced its first use of the law's amended procedures to withdraw an accelerated approval following the drug's confirmatory study failing to verify clinical benefit. Scrutiny of the accelerated approval pathway is likely to continue and may lead to legislative and/or administrative changes in the future.

Special Protocol Assessment

A company may reach an agreement with FDA under the SPA process as to the required design and size of clinical trials intended to form the primary basis of an efficacy claim. Under the FDCA and FDA guidance implementing the statutory requirement, an SPA is generally binding upon the FDA except in limited circumstances, such as if the FDA identifies a substantial scientific issue essential to determining safety or efficacy after the clinical trial begins, public health concerns emerge that were unrecognized at the time of the protocol assessment, the sponsor and FDA agree to the change in writing, or if the clinical trial sponsor fails to follow the protocol that was agreed upon with the FDA.

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 nonclinical 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, but not limited to, Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. After 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.

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 the 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 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. The agency has recently finalized guidance for industry that provides modernized recommendations for how drug manufacturers can share truthful, scientifically sound, and clinically relevant information on unapproved uses of FDA-approved drugs with health care providers.

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 ("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. The Drug Supply Chain Security

Act (the "DSCSA"), was enacted in 2013 with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States. The DSCSA mandated resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that culminated in November 2023. However, the FDA announced a one-year stabilization period, until November 2024, followed by trading partner-specific exemptions through specified dates in 2025, to give entities subject to the DSCSA additional time to finalize interoperable tracking systems and to ensure supply chain continuity. From time to time, new legislation and regulations may be implemented that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. For example, FDA released proposed regulations in February 2022 to amend the national standards for licensing of wholesale drug distributors by the states; establish new minimum standards for state licensing third-party logistics providers; and create a federal system for licensure for use in the absence of a State program, each of which is mandated by the DSCSA. It is impossible to predict whether further legislative or regulatory changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

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 ("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 ("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 an 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. The FDA's role in this process is purely "ministerial" and it does not review or assess the claims within each patent to determine whether they cover the drug product or its approved method of use. Patents that may fall outside the scope of what the FDCA and FDA's implementing regulations define as needing to be listed by the NDA holder are periodically challenged by competitors and other stakeholders, either through FDA's administrative challenge process or in the court system as anticompetitive or unfair behavior. In particular, the Federal Trade Commission ("FTC") issued a policy statement in September 2023 indicating that it would be scrutinizing the "improper" submission of patents for listing in the Orange Book on the basis that such listings may harm competition from cheaper generic alternatives and keep brand prices artificially high. The FTC followed that action in November 2023 by publicly calling out over 100 "improper" patent listings made by ten large pharmaceutical companies and initiating an FDA administrative process with respect to those patents. The controversy regarding the

appropriateness of listing such patents has led to numerous lawsuits alleging anticompetitive conduct by biopharmaceutical companies. It is unclear whether the FTC under the Trump Administration will continue to prioritize the policy issue of "improper" patent listings or whether Congress may take any legislative actions related to this issue.

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 follow-on 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 ("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 follow-on 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 qualified 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 for 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 TB*.

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 of an FDA-approved and commercially marketed drug.

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. Recent court cases have challenged FDA's approach to determining the scope of orphan drug exclusivity; however, at this time the agency continues to apply its long-standing interpretation of the governing regulations and has stated that it does not plan to change any orphan drug implementing regulations. Congress may also act to amend the law in this area at some point in the future.

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. The FDA is now 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 has finalized guidance 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 ("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 ("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 ("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 occurred on January 31, 2022. The Regulation harmonizes the assessment and supervision processes for clinical trials throughout the EU, via an EU portal and database. Under the EU Clinical Trials Regulation, a harmonized assessment and supervision processes was implemented as of January 31, 2022 for clinical trials throughout the EU, via a Clinical Trials Information System ("CTIS"). The CTIS contains the centralized EU portal and database for clinical trials conducted in the EU and will allow for a centralized review process. This harmonized submission process became mandatory for new CTA submissions as of February 1, 2023. For ongoing clinical trials, if a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation became applicable, the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

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.

The United Kingdom left the European Union on January 31, 2020 (commonly referred to as "Brexit"), with a transitional period that expired on December 31, 2020. The United Kingdom and the European Union entered into a trade agreement known as the Trade and Cooperation Agreement, which went into effect on January 1, 2021. We will continue to evaluate the potential impacts on our business of the Trade and Cooperation Agreement and guidance issued to date by the United Kingdom's Medicines and Healthcare products Regulatory Agency ("MHRA") regarding the requirements for licensing and marketing medicinal products and drugs in the United Kingdom. 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. More recently, in March 2023, the UK government and the European Commission reached agreement on a regulatory framework to replace the Northern Ireland Protocol, referred to as the Windsor Framework. The Windsor Framework is expected to apply as of January 1, 2025 and will change the existing system under the Northern Ireland Protocol, including the regulation of pharmaceutical products in the UK. Specifically, the MHRA will be responsible for approving all medicines intended to be marketed in the UK (i.e., Great Britain and Northern Ireland), while the European Medicines Agency ("EMA") will no longer be involved in approving medicines intended for sale in Northern Ireland.

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.

In April 2023, the European Commission adopted a proposal that will revise and replace the existing general pharmaceutical legislation. If implemented as currently proposed, these revisions will significantly change several aspects of drug development and approval in the European Union.

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 U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor to not cover our product candidates could reduce physician usage of the product candidate and have a material adverse effect on our sales, results of operations and financial condition. 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 pharmacy benefit managers ("PBMs") and other members of the health care and pharmaceutical supply chain, an important decision that has led to more aggressive efforts by states in this area. The Federal Trade Commission in mid-2022 also launched sweeping investigations into the practices of the PBM industry that could lead to additional federal and state legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements. During the current congressional session, numerous PBM reforms are being considered in both the Senate and the House of Representatives; they include diverse legislative proposals such as eliminating rebates; divorcing service fees from the price of a drug, discount, or rebate; prohibiting spread pricing; limiting administrative fees; requiring PBMs to report formulary placement rationale; promoting transparency. Significant efforts to change the PBM industry as it currently exists in the United States may affect the entire pharmaceutical supply chain and the business of other stakeholders, including pharmaceutical product developers like us.

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 ("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 ("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 of manufacturers that have entered into a Medicaid Drug Rebate Agreement, although such drugs may be subject to prior authorization or other utilization controls.

The U.S. Congress and state legislatures from time to time propose and adopt initiatives aimed at cost containment, which could impact our ability to sell our products profitably. For example, the federal Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, known collectively as the ACA, among other things, contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, an 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 ("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 ("ASP") to DHHS beginning on January 1, 2022, subject to enforcement via civil money penalties. The American Rescue Plan Act of 2021 also included a provision that eliminated the statutory cap on rebates that drug manufacturers pay to Medicaid. Beginning in January 2024, Medicaid rebates are no longer be capped at 100 percent of the quarterly average manufacturer price ("AMP").

In August 2022, President Biden signed into the law the Inflation Reduction Act of 2022 ("IRA"). Among other things, the IRA has multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. Starting in 2023, a manufacturer of drugs or biological products covered by Medicare Parts B or D must pay a rebate to the federal government if their drug product's price increases faster than the rate of inflation. This calculation is made on a drug product by drug product basis and the amount of the rebate owed to the federal government is directly dependent on the volume of a drug product that is paid for by Medicare Parts B or D. Additionally, starting for payment year 2026, CMS is negotiating drug prices annually for a select number of single source Part D drugs without generic or biosimilar competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. CMS has begun to implement these new authorities, entering and entered into the first set of agreements with pharmaceutical manufacturers to conduct price negotiations in October 2023 and ultimately announcing the first round of negotiated prices for the first 10 drugs in August 2024; those negotiated "maximum fair prices" will be effective as of January 1, 2026 (payment year 2026). CMS is currently engaged in its second round of negotiations and published the next 15 drugs selected for negotiation in January 2025. However, the IRA's impact on the pharmaceutical industry in the United States remains uncertain, in part because multiple large pharmaceutical companies and other stakeholders (e.g., the U.S. Chamber of Commerce) have initiated federal lawsuits against CMS arguing the program is unconstitutional for a variety of reasons, among other complaints. The outcome of such ongoing lawsuits, as well as potential legislative changes enacted by Congress or programmatic changes implemented at CMS by the Trump Administration, may impact the IRA drug price negotiation program in the future.

We expect that federal, state and local governments in the United States will continue to consider legislation directed at lowering the total cost of health care. Individual states in the United States have 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. For example, in recent years, several states have formed prescription drug affordability boards ("PDABs"). Much like the IRA's drug price negotiation program, these PDABs have attempted to implement upper payment limits on drugs sold in their respective states in both public and commercial health plans. For example, in August 2023, Colorado's PDAB announced a list of five prescription drugs that would undergo an affordability review. The effects of these efforts remain uncertain pending the outcomes of several federal lawsuits challenging state authority to regulate prescription drug payment limits.

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 (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 the individual EU Member States, nor does it have any direct consequence for pricing or reimbursement levels in the 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 ("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 the 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 the 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 the 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 federal Health Insurance Portability and Accountability Act of 1996 ("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 CMS information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain advanced non-physician health care practitioners and 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 ("HITECH") and their respective implementing regulations impose specified requirements relating to the privacy and security of individually identifiable health information that is protected under HIPAA, called "protected health information" or "PHI". HIPAA, as amended by HITECH, also requires notification to affected individuals and to federal regulators in the event of a breach of unsecured protected health information. HIPAA applies to "covered entities" or health care providers engaging in certain electronic standard transactions, such as electronic billing; health plans and healthcare clearinghouses. 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 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 third parties who acquire PHI unlawfully, 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;
- State and federal consumer protection laws, including the Federal Trade Commission Act, the Washington My Health, My Data Act, and other state privacy laws in Nevada and Connecticut govern the collection, use, disclosure and protection of health and other personal information and could apply to our operations and the operations of our collaborators; 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-U.S. 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

Healthcare Trends Affecting Pharmaceutical Pricing, Reimbursement and Access

In the United States and some foreign jurisdictions, there have been, and continue to be, legislative and regulatory policy proposals focused on controlling pharmaceutical pricing. Key issues include:

- Proposals to alter to how Medicare Part B and Part D drugs are priced and roles of the CMS in controlling growth rates, coverage, and access;
- Proposals related to the Medicare drug benefit and the role and application of manufacturer and pharmacy rebates;
- Proposals to disclosure proprietary information related to price setting, price increases and associated manufacturing and marketing expenses;
- Proposals to reduce patent and non-patent exclusivity periods; and
- State-level policy regarding pricing, access and rebates.

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.

Antimicrobial Policy

Efforts to respond to the growth of antimicrobial resistance ("AMR") have taken various forms, from non-dilutive financing of discovery, research, and development to proposals to reward innovation and enhance reimbursement. Several previous efforts in the U.S. Congress include the: Pioneering Antimicrobial Subscriptions to End Upsurging Resistance ("PASTEUR") Act that would direct large federal payments for critical need antimicrobials and the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms (DISARM) Act that would provide for separate market-rate payments for antimicrobials used in hospital settings; as well as additional funding streams provided in pandemic response efforts linked to the coronavirus. AMR remains a focus of the many policymakers internationally as well, including efforts in the United Kingdom to discover new antibacterial and a recent G7 Finance Ministers statement supporting new product development.

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 currently 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 an active pharmaceutical ingredient under cGMP conditions.

Human Capital

As of December 31, 2024, we had 32 employees, including a total of 9 employees with M.D. or Ph.D. degrees. Of these employees, 16 were primarily engaged in research and development activities, and 16 provided administrative, business and operations support. All our employees are based in the United States. None of our employees are represented by labor unions (guilds) or are covered by collective bargaining agreements. We consider our employee relations to be favorable based on our history of retention and engagement.

We hire and maintain an experienced, committed, 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 strategy. We compete with various pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions for talent and believe our success depends on our ability to attract and retain highly skilled employees. Accordingly, we offer a competitive total rewards package consisting of base salary, cash target bonus, comprehensive benefits and equity awards.

We want our employees to learn, grow and look for ways to help develop skills through industry, company and functional training and development. We offer 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, 14th Floor, 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 of 1934, as amended (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 (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. 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 occur, 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. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.

Risks Related to Product Development and Commercialization

Pursuant to our previously announced restructuring, we suspended development of our SPR720 oral program and have shifted our focus and resources to advancing the clinical development of our tebipenem HBr program, as well as other corporate activities. We have also discontinued development of SPR206. Consequently, our business and prospects are substantially dependent on our tebipenem program and our collaboration with GSK. If we fail to execute successfully on this re-prioritized strategic focus, our business and prospects may be materially adversely affected

On October 29, 2024, we announced that we suspended development activities for our SPR720 oral program based on an interim analysis of the Phase 2a proof-of-concept study of SPR720 for the treatment of NTM-PD not meeting its primary endpoint. While the data showed antimicrobial activity associated with SPR720, the interim analysis did not show sufficient separation from placebo and highlighted potential dose limiting safety issues in subjects dosed at 1,000 mg orally once daily, including three cases of reversible grade 3 hepatotoxicity. In evaluating the totality of both the efficacy and safety data, we have elected to suspend our current development program for SPR720 and continue to evaluate other potential paths forward as the remaining data are collected and analyzed. As a result, we have restructured our operations to focus on supporting the development of tebipenem HBr and other corporate activities while we continue to seek a pathway forward for SPR720. Further, in March 2025, we announced that we have discontinued development of SPR206. We believe this re-prioritized strategic focus is the best way to optimize our financial and other resources to advance our goal of developing and commercializing product candidates to address the unmet need for solutions to antibiotic resistant pathogens. However, there is no assurance that we will successfully execute this strategy. As described below, there are risks inherent in the clinical development process, especially for earlier-stage programs, and the regulatory path for SPR720 remains uncertain at this time. If we are unable to execute successfully on this re-prioritized strategic focus, our business and prospects may be materially adversely affected.

As a result, we are currently substantially dependent on our tebipenem program and our collaboration with GSK. As described under "Business—Collaboration, License and Service Agreements—Tebipenem HBr Agreements", GSK has the right to terminate the GSK License Agreement (1) at any time upon a specified number of days' notice, (2) upon a material breach by us or (3) upon a bankruptcy of Spero. Alternatively, in the case of a material breach by Spero, GSK may, in lieu of terminating the GSK License Agreement, elect to reduce any commercial milestone payments to Spero by 50%. In addition, in such circumstance, GSK may assume the responsibility and expense of development of tebipenem HBr in the United States, in which case no development milestone payments would be payable to Spero (including unpaid installments of any earned milestone payments). In the case of a Change of Control of Spero, GSK similarly may, in lieu of terminating the GSK License Agreement, assume responsibility and expense of development of tebipenem HBr in the United States and no development milestones would be payable to Spero, as described above. Any termination of the GSK License Agreement or any failure to earn, or reduction in, milestone payments may materially adversely affect our business and prospects.

Our ability to realize the value of tebipenem HBr depends on obtaining FDA approval. Even if such approval is obtained, the timeline of, and any requirements imposed as part of, such approval may impact the attractiveness of eventual commercialization of tebipenem HBr through our partnership with GSK.

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 bacterial infections causing cUTI. Our ability to realize the value of tebipenem HBr depends on the potential FDA approval, and the expected timeline and other requirements that would affect the attractiveness of eventual commercialization of tebipenem HBr through our partnership with GSK. Further, as part of any approval, the FDA could impose labeling requirements restricting the use of tebipenem HBr, which could reduce its commercial prospects, unless such requirements are subsequently modified to reduce such restrictions. If any of these outcomes occur, our business could be materially harmed.

If our clinical trials fail to 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 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.

The clinical development of any of our 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.

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 any of our 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 cause 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 ("IRBs") responsible for overseeing such trials, by the Data Safety Monitoring Board ("DSMB") if any, for such trial or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug or changes in governmental regulations or administrative actions.

If we are required to conduct additional clinical trials or other testing of any of our product candidates 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 any of our product candidates, 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 any of our product candidates.

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;
- the availability of clinically evaluable patients;
- 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 participants 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.

Congress also recently amended the FDCA to require sponsors of a Phase 3 clinical trial, or other "pivotal study" of a new drug to support marketing authorization, to design and submit a diversity action plan for such clinical trial. The action plan must describe appropriate diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. In the future, we will be required to submit a diversity action plan to the FDA by the time we submit a Phase 3 clinical trial, or pivotal study, protocol to the agency for review, unless we are able to obtain a waiver for some or all of the requirements for a diversity action plan. It is unknown at this time how the diversity action plan may affect the planning and timing of any future Phase 3 clinical trial for our product candidates. However, initiation of such trials may be delayed if the FDA objects to our proposed diversity action plans for any future Phase 3 clinical trial for our product candidates, and we may experience difficulties recruiting a diverse population of patients in attempting to fulfill the requirements of any approved diversity action plan.

Analyses of 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 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.

Analyses of preliminary or interim data from our clinical studies are not necessarily predictive of analyses of final data. Analyses of 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, analyses of interim and preliminary data should be viewed with caution until the analyses of final data are available. Adverse differences between preliminary or interim data and final data could affect our planned clinical path for any of our 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 any of our product candidates 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 IRB, 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 any of our other product candidates are associated with serious or unexpected adverse events or undesirable side effects, the FDA, the IRBs responsible for overseeing our studies, 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.

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 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 our 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 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 REMS, which may include the creation of a medication guide outlining the risks of such side effects for distribution to patients or restrictions on distribution or other elements;
- 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 any of our product candidates 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 REMS;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular infections;
- the approval of other new products for the same indications;
- the timing of market introduction of the approved product as well as competitive products;
- 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 of any of our product candidates 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 or our collaborators 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 any of our product candidates if such product candidates are approved.

To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource those functions to third parties. 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 or our collaborators 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 any of our product candidates, including the GSK License Agreement for the development and commercialization of tebipenem HBr. 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 or our collaborators 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 our 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 the product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete and noncompetitive.

There are a variety of available oral therapies marketed for the treatment of cUTIs that we would expect would compete with tebipenem HBr, if approved, 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 several IV-administered products marketed for the treatment of infections resistant to first-line therapy for Gram-negative infections, including Avycaz (ceftazidime-avibactam) from Allergan plc and Pfizer Inc., Zerbaxa (ceftolozane-tazobactam) from Merck & Co., imipenem/cilastatin and Recarbrio (relebactam) from Merck & Co., Zemdri (plazomicin) from Cipla Therapeutics, Inc., Fetroja (cefiderocol) from Shionogi & Co. Ltd., Xerava (eravacycline) from Innoviva, Inc. and Vabomere (meropenem-vaborbactam) from Melinta Therapeutics, Inc., and Exblifep (cefepime/enmetazobactam) from Allecra Therapeutics.

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.

Even if we or our partners are able to commercialize any of our product candidates, 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 any of our product candidates we develop are 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 any 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 our product candidates, if approved, which could affect their revenue potential.

Certain of our product candidates are designed to treat bacterial infections, including drug-resistant 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 any of such product candidates may develop.

For example, 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 tebipenem HBr may be marketed 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 any of our product candidates outside of controlled hospital settings, could contribute to the rise of resistance. If resistance to any of our product candidates becomes prevalent, our ability to generate revenue from 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 product candidate, tebipenem HBr, as well as exploring clinical and development pathways forward for SPR720, a key element of our strategy is to discover, develop and commercialize a portfolio of therapeutics to treat drug resistant bacterial infections. We are exploring, and intend to explore in the future, strategic partnerships for the development of new product candidates.

Research programs to identify product candidates, whether pursued internally or through strategic partnerships, 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 any of our product candidates. 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 any of our product candidates. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could adversely affect our business, financial condition, results of operations and prospects.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and

may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and wastes, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

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

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

Our internal computer systems, or those of our contract research organizations or other contractors or consultants, may fail or suffer cybersecurity incidents, 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. In particular, ransomware attacks, including those from organized criminal threat actors, nation-states and nation-state supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions, delays, or outages in our operations, loss of data, including sensitive customer information, loss of income, significant extra expenses to restore data or systems, reputational loss and the diversion of funds. To alleviate the negative impact of a ransomware attack, it may be preferable to make payments to the threat actor(s), but we may be unwilling or unable to do so, including, for example, if applicable laws or regulations prohibit such payments. Finally, developments in artificial intelligence and machine learning provide threat actors with the capability to use more sophisticated means to attack our systems and may exacerbate cybersecurity risk. 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, malware, including ransomware, software bugs, unauthorized access, natural disasters, terrorism, war, and telecommunication, equipment and electrical failures. We have measures in place that are designed to prevent, and if necessary, to detect and respond to such cybersecurity incidents and breaches of privacy and security mandates. Our measures to prevent, respond to, and minimize such risks may be unsuccessful. While we have not, to our knowledge, experienced any significant system failure, accident or material cybersecurity incident 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, as well as our financial condition. 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. Such a loss could also expose us to regulatory enforcement, civil liability and reputational damage. To the extent that any disruption or cybersecurity incident results in a loss of or damage to our data or applications, or inappropriate disclosure or theft of confidential or proprietary information, in addition to incurring liability, the further development of our product candidates could be delayed or our competitive position could be compromised. Additionally, such disruptions or cybersecurity incidents could result in enforcement actions by U.S. or foreign regulatory authorities, regulatory penalties, and other legal liabilities 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, all of which could harm our business and operations.

Our actual or perceived failure to comply with data protection laws and regulations could lead to government enforcement actions, private litigation and/or adverse publicity and could negatively affect our business.

We are subject to domestic and international data protection laws and regulations that address privacy and data security and may affect our collection, use, storage, and transfer of personal information. The legislative and regulatory landscape for data protection continues to evolve, and in recent years there has been an increasing focus on privacy and data security issues with the potential to affect our business. In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws and federal and state consumer protection laws govern the collection, use, disclosure and protection of health-related and other personal information. Failure to comply with data protection laws and regulations, where

applicable, could result in government enforcement actions, which could include civil or criminal penalties, private litigation and/or adverse publicity and could negatively affect our operating results and business. For example, California has enacted the California Consumer Privacy Act ("CCPA"), which went into effect in January of 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 the federal 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. Additionally in 2020, California voters passed the California Privacy Rights Act ("CPRA"), which went into full effect on January 1, 2023. The CPRA significantly amends the CCPA, potentially resulting in further uncertainty, additional costs and expenses in an effort to comply and additional potential for harm and liability for failure to comply. Among other things, the CPRA established a new regulatory authority, the California Privacy Protection Agency, which is tasked with enacting new regulations under the CPRA and will have expanded enforcement authority. In addition to California, more U.S. states are enacting similar legislation, increasing compliance complexity and increasing risks of failures to comply. In 2023, comprehensive privacy laws in Virginia, Colorado, Connecticut, and Utah all took effect, and laws in Montana, Oregon, and Texas took effect in 2024. Laws in a number of other U.S. states took effect, or are set to take effect, in 2025, in 2026, and beyond, and additional U.S. states have proposals under consideration, all of which are likely to increase our regulatory compliance costs and risks, exposure to regulatory enforcement action and other liabilities.

In addition, other federal and state laws establish additional requirements for protecting the privacy and security of health information that is not protected by HIPAA. For instance, Washington state recently passed the "My Health My Data" Act, which came into force in 2024 and regulates "consumer health data," which is defined as "personal information that is linked or reasonably linkable to a consumer and that identifies a consumer's past, present, or future physical or mental health." The "My Health My Data" Act provides exemptions for personal data used or shared in connection with certain research activities, including data subject to 45 C.F.R. Parts 46, 50 and 56. Notably, the "My Health My Data" Act contains a private right of action. In addition, Nevada recently enacted a consumer health data privacy bill, SB 370, which also took effect in 2024, and regulates "consumer health data." SB 370 shares many similarities with Washington's "My Health My Data" Act, and Connecticut recently amended its comprehensive privacy law to include heighted regulation of "consumer health data." Additional states may adopt health-specific privacy laws that could impact our business activities and our collection and handling of health-related data.

Numerous other countries have, or are developing, laws governing the collection, use and transmission of personal information as well. For example, the European Parliament and the Council of the European Union adopted a comprehensive general data privacy framework called the General Data Protection Regulation ("GDPR"), which took effect in May 2018 and governs the collection and use of personal data in the European Union, including by companies outside of the European Union. The GDPR, which is wide-ranging in scope, imposes 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.

Applicable data privacy and data protection laws may conflict with each other, and by complying with the laws or regulations of one jurisdiction, we may find that we are violating the laws or regulations of another jurisdiction. Despite our efforts, we may not have fully complied in the past and may not in the future. That could require us to incur significant expenses, which could significantly affect our business. Failure to comply with data protection laws may expose us to risk of enforcement actions taken by data protection authorities or other regulatory agencies, private rights of action in some jurisdictions, and potential significant penalties if we are found to be non-compliant. Furthermore, the number of government investigations related to data security incidents and privacy violations continue to increase and government investigations typically require significant resources and generate negative publicity, which could harm our business and reputation.

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

Natural disasters could severely disrupt our operations and have a material adverse effect on our business operations. If a natural disaster, health epidemic or other events beyond our control occurred that prevented us from using all or a significant portion of our office, 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 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 most years since our inception in 2013. Our net loss was $68.6 million during the year ended December 31, 2024. All of our product candidates are in development, none have been approved for sale and we may never have a product candidate approved for commercialization.

In accordance with Accounting Standards Update ("ASU") 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205- 40), we have evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern within one year after the date that these consolidated financial statements are issued. Based on our cash and cash equivalents as of December 31, 2024, together with earned and non-contingent development milestone payments from GSK, as well as other non-dilutive funding commitments, we believe that our cash runway will be sufficient to fund our operating expenses and required capital expenditures into the second quarter of 2026. During this period, we plan to prioritize advancing the Phase 3 clinical trial activities for tebipenem HBr under our GSK License Agreement and completing our analysis of the full dataset from the 25 treated patients in the Phase 2a proof-of-concept trial of SPR720. Beyond this point we will need additional funding, which we expect will primarily consist of raising additional capital through some combination of equity or debt financings, potential new collaborations or additional grant funding. If we are not able to secure adequate additional funding, we plan to make further reductions in spending. In that event, we may have to delay, scale back, or eliminate some or all of our planned development 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 expect to continue to incur significant expenses and 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 operating losses for the foreseeable future as we continue to advance our product candidates through preclinical and clinical development and marketing approval for such candidates whose 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 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, face competing technological and market developments; and
- acquire or in-license other product candidates and technologies.

We currently have no products approved for sale and have historically invested a significant portion of our efforts and financial resources on the development of our product candidates, including tebipenem HBr, SPR206, and SPR720. Although we have decided to discontinue further development of SPR206 and are exploring strategic options, including potential out-licensing, to maximize the value for the program and allow us to leverage the expertise of strategic partners and have suspended our current development efforts with respect to the SPR720 oral program, although we continue to evaluate other potential paths forward as the remaining data are collected and analyzed, our business remains heavily dependent on the successful development, regulatory approval, and, if approved, commercialization of tebipenem HBr and other future product candidates. We cannot be certain that any product candidate will receive regulatory approval or will be successfully commercialized even if it receives regulatory approval.

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 payments under our government awards or from our commercial partnership agreements, we could be forced to delay, reduce or eliminate our product development programs.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete. Our expenses are likely to increase as we commence and advance our ongoing and planned clinical trials and other studies for our current and future product candidates, as well as explore clinical and development pathways forward for SPR720. If we obtain marketing approval for any product candidate, we expect to incur significant expenses related to development, 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.

Based on our cash and cash equivalents as of December 31, 2024, together with earned and non-contingent development milestone payments from GSK, as well as other non-dilutive funding commitments, we believe that our cash runway will be sufficient to fund our operating expenses and capital expenditures into the second quarter of 2026. During this period, we plan to prioritize advancing the Phase 3 clinical trial activities for tebipenem HBr under our GSK License Agreement and completing our analysis of the full dataset from the 25 treated patients in the Phase 2a proof-of-concept trial of SPR720. Beyond this point we will need additional funding, which we expect will primarily consist of raising additional capital through some combination of equity or debt financings, potential new collaborations or additional grant funding. If we are not able to secure adequate additional funding, we plan to make further reductions in spending. In that event, we may have to delay, scale back, or eliminate some or all of our planned development activities, including:

- the timing and terms of the potential FDA approval of tebipenem HBr;
- 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 our product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- 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.

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

Unless and until we can generate a substantial amount of revenue from our product candidates, we expect to finance our future cash needs through public or private equity offerings, debt financings, collaborations, licensing arrangements and government funding arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. We filed a universal shelf registration statement on Form S-3 (Registration No. 333-254170) with the SEC on March 11, 2021, which was declared effective on March 29, 2021 (the "2021 Form S-3"), and pursuant to which we registered 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 could determine, including up to $75.0 million of our common stock available for issuance pursuant to the Controlled Equity Offering Sales Agreement (the "Sales Agreement") that we entered into with Cantor Fitzgerald & Co. ("Cantor"). The 2021 Form S-3 expired on March 29, 2024.

We filed a new universal shelf registration statement on Form S-3 (Registration No. 333-277998) with the SEC on March 15, 2024, which became effective on March 22, 2024 and pursuant to which we registered 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 the Sales Agreement with Cantor. Under the Sales Agreement, Cantor may sell shares of our common stock by any method permitted by law deemed to be an "at-the-market" offering as defined in Rule 415 of the Securities Act of 1933, as amended (the "Securities Act"), subject to the terms of the Sales Agreement.

While we currently have an effective shelf registration statement, as of the filing of this Annual Report on Form 10-K, our public float is less than $75 million, and under SEC regulations for so long as our public float remains less than $75 million, the amount we can raise through primary public offerings of securities in any twelve-month period using shelf registration statements is limited to an aggregate of one-third of our public float, which is referred to as the baby shelf rules. As of March 21, 2025, our public float was approximately $45.1 million, based on 54,969,832 shares of outstanding common stock held by non-affiliates and at a price of $0.82 per share, which was the closing price of our common stock on the Nasdaq Global Select Market ("Nasdaq GS") on March 21, 2025. As a result of our public float being below $75 million, we will be limited by the baby shelf rules until such time our public float exceeds $75 million, which means we only have the capacity to sell shares up to one-third of our public float in primary offerings under our shelf registration statement on Form S-3 in any twelve-month period. Although alternative public and private transaction structures may be available, these may require additional time and cost, may impose operational restrictions on us, and may not be available on attractive terms.

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, 2024, we had U.S. federal, state and foreign net operating loss carryforwards ("NOLs") of $165.2 million, $120.6 million and $4.6 million, respectively. $152.0 million of the federal NOLs can be carried forward indefinitely and $13.2 million of the federal NOLs begin to expire in 2034. The state NOLs begin to expire in 2034 and will expire at various dates through 2044. The foreign NOLs do not expire. Utilization of these NOLs depends on many factors, including our future income, which cannot be assured. Aside from the NOLs that can be carried forward indefinitely, the remaining 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 (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 recently completed a Section 382 study and concluded that we underwent several ownership changes as defined by the Code, the last of which occurred during the year ended December 31, 2018. Any carryforwards that will expire prior to utilization were removed from deferred tax assets, with a corresponding reduction of the valuation allowance. Future ownership changes may limit our ability to utilize remaining tax attributes.

Under current U.S. federal tax legislation, although the treatment of NOLs arising in tax years beginning on or before December 31, 2017 has generally not changed, NOLs 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.

Our operations to date have been limited to financing and staffing our company, and performing research and development activities to advance our product candidates. Each of our product candidates is either in clinical or preclinical development. 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 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 Our Dependence on Third Parties

We may not achieve the milestones triggering payments to us in our license and collaboration agreements with third parties.

We have and may continue to seek third-party collaborators for development and commercialization of certain of our product candidates. Currently we are party to license and collaboration agreements with third parties as described in Note 13 (“License, Collaboration and Service Agreements”) to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. 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 not be able to develop, manufacture, market and sell our product candidates and use our intellectual property without infringing or misappropriating the intellectual property and other proprietary rights of third parties;
- 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 our 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 nonclinical 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 our 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 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 our 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 our 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 our 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 and one supplier 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.

In addition, because some of our manufacturers have manufacturing facilities in Taiwan, their ability to provide us with adequate supplies of high-quality products on a timely and cost-efficient basis is subject to a number of additional risks and uncertainties, including political, social and economic instability and factors that could impact the shipment of supplies. If our manufacturers are unable to provide us with adequate supplies of high-quality products on a timely and cost-efficient basis, our operations would be disrupted and our net revenue and profitability would suffer.

Our third-party contract manufacturers are based in Asia. Recently, our third-party contract manufacturers have been subject to various supply chain disruptions. These supply chain disruptions have increased the price of certain materials due to the significant increase in costs of raw materials and shipping costs. Our ability to produce and timely deliver our products may be materially impacted in the future if these supply chain disruptions continue or worsen.

Further, a major catastrophe, such as an earthquake or other natural disaster, labor strike, or work stoppage at any of our manufacturing facilities, or a manufacturing facility of our suppliers or customers, could result in a prolonged interruption of our business. A disruption resulting from any one of these events could cause significant delays in shipments of our products and the loss of revenue and customers, which could have a material adverse effect on our financial position, results of operations, and cash flows. Our facilities in Japan and Taiwan are located in seismically-active areas.

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 our 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 out-license acquire development or commercialization rights to products, technology or data from or to third parties, we could lose such rights that are important to our business.

We are a party to agreements with Meiji and GSK for tebipenem HBr, Vertex Pharmaceuticals for SPR720 and Pfizer, Everest 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 the Meiji License that gives us rights outside of the Meiji Territory 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 the Meiji Territory. In addition, we have the right to develop, manufacture and have manufactured tebipenem HBr in the Meiji Territory solely for the purpose of furthering development, manufacturing and commercialization of tebipenem HBr outside of the Meiji Territory. 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 $1.0 million upon the achievement of specified regulatory milestones and royalties of a low single-digit percentage on net sales on a country-by-country basis.

In addition, pursuant to our GSK License Agreement, we granted GSK an exclusive royalty-bearing license, with the right to grant sublicenses, under our intellectual property and regulatory documents and a sublicense under certain intellectual property of Meiji and Meiji's regulatory documents to develop, manufacture and commercialize the GSK Licensed Products in the GSK Territory. Under the terms of the GSK License Agreement, we received an upfront payment of $66.0 million for GSK to secure rights to the medicine, a $30.0 million milestone payment upon achievement of a development milestone in the third quarter of 2023, and are entitled to receive a $95.0 million development milestone that is payable in four equal semi-annual installments, of which we received $23.8 million in February 2024, $23.8 million in August 2024 and $23.8 million in February 2025. Remaining potential payments under the GSK License Agreement are milestone based and are (i) approximately $25.0 million in payments for GSK's submission of a NDA with the FDA for tebipenem HBr, (ii) up to $150.0 million in commercial milestone payments, (iii) up to $225.0 million in sales milestone payments, and (iv) tiered low single-digit to low double-digit royalties (if sales exceed $1.0 billion) tiered on net sales of GSK Licensed Products in the GSK Territory.

We are responsible for the execution and costs of the follow-up Phase 3 clinical trial of tebipenem HBr. GSK is responsible for the execution and costs of additional further development, including Phase 3 regulatory filing and commercialization activities for tebipenem HBr in the balance of the GSK Territory outside of the United States. We will also be responsible for providing and paying for the clinical supply of tebipenem HBr while GSK will be responsible for the costs of the commercial supply of tebipenem HBr.

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

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

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

We have received significant non-dilutive financing from various government agencies for the further development of our product candidates. Such funding sources may pose risks to us not encountered in other commercial contracts, including significant regulatory compliance risks. Contracts funded by the 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 U.S. manufacturing requirements for products that embody inventions conceived or first reduced to practice under such agreements;
- suspend or debar the contractor or grantee from doing future business with the government;
- control and potentially prohibit the export of products; and
- pursue criminal or civil remedies under the False Claims Act (the "FCA"), the False Statements Act and similar remedy provisions specific to government agreements.

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

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

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

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

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

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

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

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

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

United States government agencies such as the DHHS and the Defense Contract Audit Agency (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 (the "FAR") and agency-specific regulations supplemental to the FAR, which comprehensively regulate the procurement, formation, administration and performance of government contracts;
- business ethics and public integrity obligations, which govern conflicts of interest and the hiring of former government employees, restrict the granting of gratuities and funding of lobbying activities and include other requirements such as the Anti-Kickback Statute and the Foreign Corrupt Practices Act;

- export and import control laws and regulations; and
- laws, regulations and executive orders restricting the use and dissemination of information classified for national security purposes and the exportation of certain products and technical data.

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

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

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

Risks Related to Our Intellectual Property

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

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

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds and technologies commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Furthermore, 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 United States, 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 pre-issuance 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.

Due to the war in Ukraine and sanctions between the United States and Russia, patents and patent applications in Russia, the EAPO and Ukraine currently have an uncertain fate. Unless the conflict with Ukraine ends quickly it is unlikely our Russian and EAPO patent and patent applications will remain in effect. Ukraine is currently under martial law and not processing patent applications. It is expected all patent deadlines in Ukraine will be extended.

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 ANDAs to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable and/or not infringed. Alternatively, our competitors may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid and/or unenforceable. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

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

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

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

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

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

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

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our technology or product candidates, including interference proceedings before the 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 and regulatory documents concerning tebipenem pivoxil, we are neither a party to, nor an express third-party beneficiary of, the letter agreements, which were signed in January 2017 and in February 2022, between Meiji and Global Pharma consenting to Meiji's arrangements with us. As such, if any dispute among the parties were to occur, our direct enforcement rights with respect to the letter agreements may be limited or uncertain.

If we are found to infringe a third party's intellectual property rights, we or our third-party collaborators could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we or they 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 or such collaborators 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 or our third-party collaborators have misappropriated the intellectual property, 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, 2024, we have two registered U.S. trademarks, 23 registered foreign trademarks, and no pending foreign 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 jurisdictions, 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 applied to register our product candidate name as a trademark in the United States, where it has been allowed for registration, and have applied to register the mark in three foreign jurisdictions. We have also applied to register additional product candidate names as trademarks in the United States. 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 USPTO 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 any 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 our 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 have only limited experience in filing and supporting the applications necessary to gain marketing approvals and have relied 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 product candidates we 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.

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. 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 a 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 cUTIs, including pyelonephritis, in adult patients who have limited oral treatment options, as well as fast track designation for SPR720 for treatment of adult patients with NTM pulmonary disease, 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.

Priority review designation by the FDA may not lead to a faster regulatory review or approval process and, in any event, does not assure FDA approval.

If the FDA determines that a product candidate intended to treat a serious disease, if approved, would provide a significant improvement in safety or effectiveness of the treatment of the disease, the FDA may designate the drug application for that product candidate for priority review. A priority review designation means that the goal for the FDA to review the marketing application is six months from the date of NDA acceptance for filing, rather than the standard review period of ten months from the date of NDA acceptance for filing. A priority review designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving a priority review designation from the FDA does not guarantee approval of the drug application within the six-month review cycle or any time thereafter.

While we have negotiated a SPA agreement with the FDA relating to our pivotal Phase 3 clinical trial of tebipenem HBr in patients with cUTI, including AP, this agreement does not guarantee approval of tebipenem HBr or any other particular outcome from regulatory review of the clinical trial or the product candidate.

On July 31, 2023, the Company announced that it received written agreement from the FDA, under a SPA, on the design and size of PIVOT-PO, a pivotal Phase 3 clinical trial of tebipenem HBr in patients with cUTI, including AP. The FDA's SPA process is designed to allow the FDA to evaluate the proposed design and size of clinical trials that are intended to form the primary basis for determining a drug product's efficacy, among other eligible protocols. Upon specific written request by a clinical trial sponsor, the FDA will evaluate the planned protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis. The FDA ultimately assesses whether the protocol design and planned analysis of the trial adequately address scientific and regulatory requirements for the particular purposes identified by the sponsor, which in this case was that the PIVOT-PO protocol can be considered an adequate and well-controlled study in support of our future resubmission of the tebipenem HBr marketing application. All agreements between the FDA and the sponsor regarding an SPA must be clearly documented in writing, either in the form of an SPA letter or minutes of a meeting between the sponsor and the FDA at which the SPA agreement was reached.

However, an SPA agreement does not guarantee approval of a product candidate, and even if the FDA agrees to the design, execution and analysis proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, an SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, if other new scientific concerns regarding product safety or efficacy arise, if the sponsor fails to comply with the agreed upon trial protocols or modifies such protocols without prior FDA agreement, or if the relevant data, assumptions or information provided by the sponsor change or are found to be false or omit relevant facts. In addition, even after an SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, so long as the FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study.

The FDA retains significant latitude and discretion in interpreting the terms of an SPA agreement, as well as the data and results obtained from any study that is the subject of the SPA agreement. We cannot assure you that our pivotal Phase 3 clinical trial will succeed, or that the SPA agreement will ultimately be binding on the FDA or will result in any FDA approval of tebipenem HBr. We expect that the FDA will review our compliance with the protocol that is subject to the SPA agreement, and, as with all NDA reviews, evaluate the results of the trial and conduct inspections of some of the sites where the trial will be conducted. We cannot assure you that the FDA will deem each of the clinical trial sites to have complied with applicable laws and regulations, and negative inspection results could significantly delay or prevent any potential approval for tebipenem HBr. If the FDA revokes or alters its agreement under the SPA, or interprets the data collected from the clinical trial differently than we do, the FDA may not deem the data sufficient to support an application for regulatory approval, which could materially adversely affect our business, financial condition and results of operations.

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 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 ANDAs. An ANDA relies on the preclinical and clinical testing conducted for a previously approved reference listed drug ("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 ultimately approves tebipenem HBr for the treatment of cUTI, including pyelonephritis, caused by certain microorganisms in adult patients who have limited oral treatment options, 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 qualified infectious disease product 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 or our partners 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 our product candidates in the European Union and many other jurisdictions, we or our partners 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. Further, in April 2023, the European Commission issued a proposal to revise and replace the existing general pharmaceutical legislation. If adopted and implemented as currently proposed, these revisions will significantly change several aspects of drug development and approval in the European Union. 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 or our partners 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 of our product candidates, 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. 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;
- 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 services involving the use or disclosure of protected health information, including mandatory contractual terms, with respect to safeguarding the privacy and security of protected health information, and requires notification to affected individuals and regulatory authorities of certain breaches of security of protected 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 Physician Payments Sunshine Act requires manufacturers of drugs, devices, biologics and medical supplies covered by Medicare or Medicaid to report, on an annual basis, to the DHHS, information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, chiropractors and certain advanced non-physician health care practitioners), teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- state and federal consumer protection laws, including the Federal Trade Commission Act, govern the collection, use, disclosure and protection of health and other personal information and could apply to our operations and the operations of our collaborators; 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, do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If governmental authorities find that our operations violate any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, imprisonment, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and we may be required to curtail or restructure our operations. Moreover, we expect that there will continue to be federal and state laws and regulations, proposed and implemented, that could affect our operations and business. The extent to which future legislation or regulations, if any, relating to healthcare fraud and abuse laws or enforcement, may be enacted or what effect such legislation or regulation would have on our business remains uncertain.

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

The pricing and reimbursement environment may become more challenging due to, among other reasons, policies advanced by the 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.

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 ("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%. As long as these cuts remain in effect, they could adversely affect payment for our product candidates, if approved for commercial marketing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. There have been several 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 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. The Federal Trade Commission in mid-2022 also launched sweeping investigations into the practices of the PBM industry, and published interim reports with its finding in mid-2024 and January 2025, that could lead to additional federal and state legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements, including in the current 2025-2026 congressional session. During the previous congressional session, numerous bipartisan PBM reforms were considered in both the Senate and the House of Representatives; they include diverse

legislative proposals such as eliminating rebates; divorcing service fees from the price of a drug, discount, or rebate; prohibiting spread pricing; limiting administrative fees; requiring PBMs to report formulary placement rationale; promoting transparency. Significant efforts to change the PBM industry as it currently exists in the United States may affect the entire pharmaceutical supply chain and the business of other stakeholders, including biopharmaceutical developers like us. In September 2023, the FTC issued a policy statement articulating its view that certain "improper" patent listings by drug developers in FDA's Orange Book represent an unfair trade practice and indicated that industry should be prepared for potential enforcement actions based on its analysis. The FTC followed that action in November 2023 by publicly calling out over 100 "improper" patent listings made by ten large pharmaceutical companies and initiating an FDA administrative process with respect to those patents. The controversy regarding the appropriateness of listing such patents has led to numerous lawsuits alleging anticompetitive conduct by biopharmaceutical companies. It remains to be seen whether the FTC under the Trump Administration will continue to prioritize the policy issue of "improper" patent listings or whether Congress may take any legislative actions related to this issue. Accordingly, regulatory and government interest in biopharmaceutical industry business practices continues to expand and pose a risk of uncertainty.

Further, in August 2022, President Biden signed into the law the IRA. Among other things, the IRA has multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. A manufacturer of drugs covered by Medicare Parts B or D must now pay a rebate to the federal government if their drug product's price increases faster than the rate of inflation. This calculation is made on a drug product by drug product basis and the amount of the rebate owed to the federal government is directly dependent on the volume of a drug product that is paid for by Medicare Parts B or D. Additionally, starting for payment year 2026, CMS will negotiate drug prices annually for a select number of single source Part D drugs without generic or biosimilar competition. CMS is negotiating drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. CMS has begun to implement these new authorities, entering into agreements to conduct negotiations with the relevant manufacturers of those selected drugs in October 2023 and ultimately announcing the first round of negotiated prices for the first 10 drugs in August 2024; those negotiated "maximum fair prices" will be effective as of January 1, 2026 (payment year 2026). CMS is currently engaged in its second round of negotiations and published the next 15 drugs selected for negotiation in January 2025. However, the impact of this program on the biopharmaceutical industry in the United States remains uncertain, in part because multiple large pharmaceutical companies and other stakeholders (e.g., the U.S. Chamber of Commerce) have initiated federal lawsuits against CMS arguing the program is unconstitutional for a variety of reasons, among other complaints. The outcome of such ongoing lawsuits, as well as potential legislative changes enacted by Congress or programmatic changes implemented at CMS by the Trump Administration, may impact the IRA drug price negotiation program in the future.

Legislative and regulatory proposals also 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.

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.

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

If we participate in the Medicaid Drug Rebate Program if and when we successfully commercialize a product candidate, we will be required to report certain pricing information for our product to the Centers for Medicare & Medicaid Services, the federal agency that administers the Medicaid and Medicare programs. We may also be required to report pricing information to the 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 ASP to DHHS beginning on January 1, 2022, subject to enforcement via civil money penalties. Increasingly there are state laws and regulations that require prescription drug price reporting or impose other restrictions designed to control pharmaceutical product pricing, such as price or patient reimbursement constraints and discounts.

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.

Disruptions of funding for the FDA, the SEC and other government agencies caused by funding shortages, mass layoffs, or global health concerns 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 during that period. In early 2025, following the inauguration of President Trump, the Trump Administration began terminating federal government employees, including at the FDA. The impact of mass layoffs at the agency and other governmental offices with which we interact is unclear at this time. However, it is expected that with a proposed reduction in staff of up to 50%, the FDA in the future may be unlikely to meet its application review goals or to continue to be available for timely interactions with medical product developers. It is currently unclear how the U.S. biopharmaceutical industry will be affected by the Trump Administration's major changes to the FDA and the federal government as a whole.

Separately, during the COVID-19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the agency has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates, and any resurgence of the virus or emergence of new infectious disease outbreaks may lead to future inspectional delays. Regulatory authorities outside the United States may adopt similar policy measures in response to emerging infectious disease outbreaks, epidemics, or pandemics. If a prolonged government shutdown or slowdown occurs, or if global health concerns similar to COVID-19 prevent the FDA or other regulatory agencies from conducting their regular inspections, review, or other regulatory activities, 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.

Further, three decisions from the U.S. Supreme Court issued in July 2024 may lead to an increase in litigation against regulatory agencies that could create uncertainty and thus negatively impact our business. The first decision overturned established precedent that required courts to defer to regulatory agencies' interpretations of ambiguous statutory language. The second decision overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. The third decision extended the statute of

limitations within which entities may challenge agency actions. These cases may result in increased litigation by industry against regulatory agencies, including but not limited to the FDA and SEC, and may impact how such agencies choose to pursue enforcement and compliance actions. However, the specific, lasting effects of these decisions, which may vary within different judicial districts and circuits, is unknown. We also cannot predict the extent to which FDA and SEC regulations, policies, and decisions may become subject to increasing legal challenges, delays, and changes.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our 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 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.

On October 29, 2024, we implemented a restructuring plan that will reduce our workforce by approximately 39%. While we have confidence in our remaining employees, including our leadership team, and the Board of Directors, the uncertainty inherent in this ongoing restructuring may be difficult to manage, may cause concerns from third parties with whom we do business, and may increase the likelihood of turnover of other key officers and employees. Continued disruption caused by the transition or by the loss of ongoing services of any qualified scientific and management personnel could delay or prevent the successful development of our product candidates.

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 undertook internal restructuring activities that could result in disruptions to our business or otherwise materially harm our results of operations or financial condition, and we may not realize the expected benefits from our restructuring and we may incur additional costs implementing it or other difficulties.

On October 29, 2024, we announced a restructuring plan and implemented a workforce reduction. There can be no assurance that our restructuring will achieve the cost savings, operating efficiencies or other benefits that we may initially expect. Restructuring activities may also result in a loss of continuity, accumulated knowledge and inefficiency during transitional periods and thereafter. Further, internal restructurings can require a significant amount of time and focus from management and other employees, which may divert attention from operations. Additionally, our restructuring may result in unexpected expenses or liabilities and/or write-offs. If our restructuring fails to achieve some or all of the expected benefits therefrom, our cash resources may not last as long as estimated and our business, results of operations and financial condition could be materially and adversely affected.

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 conflicts, 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.

Risks Related to Our Common Stock

The price of our common stock has been and, in the future, may continue to be volatile whether related or unrelated to our operations, which could result in a decline in value 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 any of our product candidates;
- 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.

An active trading market for our common stock may never develop or be sustained.

Although our common stock is listed on the Nasdaq GS, an active trading market for our shares may never develop or be sustained. As a result, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares, or at all.

Our shares of common stock could be delisted from the Nasdaq GS, which could result in, among other things, a decline in the price of our common stock and less liquidity for our stockholders.

Our common stock is listed on the Nasdaq GS, which imposes, among other requirements, a minimum $1.00 per share bid price requirement for continued inclusion on the Nasdaq GS pursuant to Nasdaq Listing Rule 5450(a)(1) (the "Bid Price Requirement"). The closing bid price for our common stock must remain at or above $1.00 per share to comply with the Bid Price Requirement for continued listing. On February 25, 2025, we received a deficiency letter (the "Notice") from the Listing Qualifications Department of Nasdaq, or the Nasdaq Staff, informing us that we were not in compliance with the continued listing requirements of the Nasdaq GS because the bid price for our common stock had closed below $1.00 per share for 30 consecutive trading days. In accordance with Nasdaq Listing Rule 5810(c)(3)(A), we have until August 25, 2025 (the "Compliance Date"), to regain compliance with the Bid Price Requirement.

According to the Notice, if at any time before August 25, 2025, the closing bid price of our common stock is at least $1.00 per share for a minimum of 10 consecutive business days, Nasdaq will provide written notification that we have achieved compliance with the Bid Price Requirement and our common stock will continue to be eligible for listing on the Nasdaq GS. If we do not regain compliance with the Bid Price Requirement by the Compliance Date, we may be eligible for an additional 180 day compliance period under the following circumstances. To qualify, we would need to transfer the listing of the common stock to the Nasdaq Capital Market, provided that we meet the continued listing requirement for the market value of publicly held shares and all other initial listing standards, with the exception of the Bid Price Requirement. To effect such a transfer, we would also need to pay an application fee to Nasdaq and will need to provide written notice to Nasdaq of our intention to cure the deficiency during the additional compliance period by effecting a reverse stock split, if necessary. As part of its review process, Nasdaq would make a determination of whether it believes we will be able to cure this deficiency.

If Nasdaq concludes that we will not be able to cure the deficiency, or if we do not cure the deficiency within such additional 180 day compliance period, Nasdaq will provide written notification to us that our common stock will be subject to delisting. At that time, we may appeal Nasdaq's delisting determination to a Nasdaq Listing Qualifications Panel (the "Panel"). However, there can be no assurance that, if we receive a delisting notice and appeal the delisting determination by Nasdaq to the Panel, such appeal would be successful.

There can be no assurance that we will be able to keep the closing bid price above $1.00 per share for the required 10 consecutive trading days by August 25, 2025. Further, if we are unable to maintain the closing bid price at $1.00 for the required period, there is no guarantee that we will regain compliance with the Bid Price Requirement. There is no guarantee that a reverse stock split would be approved by the stockholders or that a reverse stock split would allow us to regain compliance with the Bid Price Requirement.

Any potential delisting of our common stock could have a material adverse effect on the market for, and liquidity and price of, our common stock and would adversely affect our ability to raise capital on terms acceptable to us, or at all. Delisting from Nasdaq GS could also have other negative results, including, without limitation, the potential loss of confidence by investors, customers and employees and fewer business development opportunities. Such a delisting from the Nasdaq GS would also make trading our common stock more difficult for stockholders to sell their shares in the public market. We intend to actively monitor the closing bid price of our common stock and may, if appropriate, consider implementing available options to maintain compliance with the minimum bid price requirement under the Nasdaq Listing Rules.

We intend to actively monitor the closing bid price of our common stock and may, if appropriate, consider implementing available options to regain compliance with the minimum bid price requirement under the Nasdaq Listing Rules.

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.

Unstable global economic and political conditions, including economic uncertainty tied to volatility in interest rates and inflation, credit and financial market instability, and uncertainty related to ongoing geopolitical conflicts, could adversely affect our business, financial condition, stock price and ability to raise capital.

Unstable global economic and political conditions, including economic uncertainty tied to volatility in interest rates and inflation, credit and financial market instability, and uncertainty related to ongoing geopolitical conflicts, could adversely affect our business, financial condition, stock price and ability to raise capital. The global economy, in particular the financial markets, have recently experienced significant disruption and volatility, including without limitation, as a result of volatility in interest rates and inflation, capital markets volatility, currency rate fluctuations, volatility in commodity prices, decline in consumer confidence and economic growth, supply chain disruptions, banking disruptions, and uncertainty resulting from geopolitical events, including trade wars, civil and political unrest, wars and other armed conflicts. In addition, market, interest rate, and inflation volatility may increase our cost of financing or restrict our access to potential sources of future capital. Furthermore, our stock price may further decline due in part to the volatility of the stock market and any general economic downturn.

If the disruption and volatility persist or heighten, it may impact our ability to raise sufficient additional capital on agreeable terms, if at all. If we are unable to raise sufficient additional capital, our business, financial condition, stock price and results of operations could be adversely affected, and we will need to implement cost reduction strategies, which could include delaying, reducing or altogether terminating both internal and external costs related to our operations and research and development programs. In addition, political developments impacting government spending and international trade, including changes in trade agreements, trade disputes, tariffs and investment restrictions, such as the ongoing trade dispute between the United States and China, may negatively impact markets and cause weaker macroeconomic conditions. These global economic and political factors could also strain certain of our suppliers and manufacturers, possibly resulting in supply disruptions or increased raw material or manufacturing costs, or adversely impacting their ability to manufacture clinical trial materials for our product candidates. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic and geopolitical climate and financial market conditions could adversely impact our business.

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

Our management has 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 a smaller reporting company and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

We are subject to Section 404 of The Sarbanes-Oxley Act of 2002 ("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. However, for so long as we remain 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 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 continue to qualify as a SRC and non-accelerated filer if the market value of our common stock held by non-affiliates is below $75.0 million (or $700.0 million if our annual revenue is less than $100.0 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 compliance initiatives and corporate governance practices.

As a public 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 GS 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 at any time, 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, 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.

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, as amended, and Amended and Restated Bylaws 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 Amended and Restated Certificate of Incorporation, as amended, or Amended and Restated Bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law (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, as amended, 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, as amended, 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 Amended and Restated Certificate of Incorporation, as amended, 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 Amended and Restated Certificate of Incorporation, as amended, 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.

We have received a "Wells Notice" from the SEC contemplating a civil enforcement action, which could have a material adverse effect on our business, financial condition and results of operations, prospects, and/or our stock price.

On January 9, 2025, we responded to a "Wells Notice" from the staff of the Boston Regional Office (the "Staff") of the SEC regarding its preliminary determination to recommend a civil enforcement action or administrative proceeding against us, its former Chief Executive Officer and Chairman of the Board of Directors, Ankit Mahadevia, M.D. ("Dr. Mahadevia"), and its former Chief Financial Officer and President and Chief Executive Officer, Satyavrat "Sath" Shukla ("Mr. Shukla"), relating to certain public disclosures by us from March 31, 2022 leading up to our announcement on May 3, 2022 that we had determined to cease commercialization of tebipenem HBr based on feedback from the FDA, and whether our disclosures may have violated the federal securities laws (the "Investigation").

A Wells Notice is neither a formal charge of wrongdoing nor a final determination that the recipient has violated any law, but is a preliminary determination by the Staff to recommend to the SEC Commissioners that a civil enforcement action or administrative proceeding be brought against the recipients. If the SEC were to authorize an action against us and/or any of the identified individuals, it may seek an injunction or cease-and-desist order against future violations of provisions of the federal securities laws, the imposition of civil monetary penalties, disgorgement or other equitable relief within the SEC's authority, or any combination of the foregoing. The SEC could also seek an order barring each identified individual from serving as an officer or director of a public company for a specified period of time.

We, Dr. Mahadevia and Mr. Shukla are cooperating with the SEC and have made a submission in response to the Wells Notice explaining why an enforcement action would not be appropriate. We cannot predict the results of the Investigation and the Wells Notice process and any corresponding enforcement action against us and/or any of the identified individuals, and the costs, timing and other potential consequences of responding and complying therewith with any certainty. The Investigation, and the Wells Notice process continues to be expensive and disruptive, and we are subject to indemnifying each of the individuals for their costs associated with the Wells Notices. Our insurance, to the extent maintained, may not cover all claims that may be asserted against us or the

specified individuals, and we are unable to predict how long the Investigation will continue. An unfavorable outcome may have an adverse impact on our business, financial condition and results of operations, prospects, or our stock price. Any proceeding could also negatively impact our reputation among our stakeholders.

We may become involved in securities litigation that could divert management's attention and harm the company's business, and insurance coverage may not be sufficient to cover all costs and damages.

In the past, securities litigation has often followed certain significant business activities, such as the announcement of a strategic restructuring, or the announcement of negative events, such as negative results from clinical trials. We may be exposed to such litigation even if no wrongdoing occurred. Litigation is usually expensive and diverts management's attention and resources, which could adversely affect our business and cash resources and our ability to execute on our partnership with GSK to eventually commercialize tebipenem HBr, or the ultimate value our stockholders receive in such partnership or other opportunity.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Cybersecurity Strategy

We have established and currently maintain processes designed to assess, identify and manage risks from cybersecurity threats to, among other things, our critical computer networks, third party hosted services, communications systems, and our critical and sensitive data. These cybersecurity processes are designed to secure our networks and information systems and protect our operations and information assets from unauthorized access or attack. Such cybersecurity processes include technical, procedural and organizations safeguards that are built into our overall information technology ("IT") function. Our Board of Directors is actively involved in oversight of our risk management activities, and cybersecurity represents an important element of our overall approach to risk management. As discussed in more detail under "Cybersecurity Governance" below, the audit committee of our Board of Directors provides oversight of our cybersecurity risk management and strategy processes, led by our Head of IT.

Our approach to cybersecurity is tailored to suit the specific environment in which we operate and is based on recognized frameworks established by applicable industry standards. In general, we seek to address cybersecurity risks through a comprehensive, cross-functional approach that is focused on preserving the confidentiality, security and availability of the information that we collect and store by identifying, preventing and mitigating cybersecurity threats and effectively responding to cybersecurity incidents when they occur. Our approach includes a comprehensive strategy featuring a risk management team lead by our Head of IT and a regularly tested incident response plan. We also identify our cybersecurity threat risks by comparing our processes to industry standards, as well as by engaging third party experts to conduct risk assessments, tabletop exercises, threat modeling, and vulnerability testing.

Our incident response plan coordinates the activities we take to prepare for, detect, respond to and recover from cybersecurity incidents, which include processes to triage, assess severity for, escalate, contain, investigate and remediate the incident, as well as to comply with potentially applicable legal obligations and mitigate damage to our business and reputation. Our incident response plan requires that suspected cybersecurity incidents are promptly reported to our Controller and Chief Human Resource Officer and includes an escalation path to our Chief Executive Officer, executive leadership team, and Board of Directors.

In the last three fiscal years, we have not experienced any material cybersecurity incidents and are not aware of any cybersecurity incidents at third parties with whom we conduct business that may have impacted us.

Cybersecurity Management

Cybersecurity is an important part of our risk management processes and an area of focus for our Board of Directors and management. In general, our Board of Directors oversees risk management activities designed and implemented by our management. Our Board of Directors executes its oversight responsibility for risk management both directly and through delegating oversight of certain of these risks to its committees, and our Board of Directors has authorized our audit committee to oversee risks from cybersecurity threats.

Our audit committee receives periodic updates from management on our cybersecurity processes. The audit committee receives information regarding current and emerging material cybersecurity threat risks and our ability to mitigate those risks. Our Board of Directors receives prompt and timely information regarding any cybersecurity incident that meets established reporting thresholds, as well as ongoing updates regarding any such incident until it has been addressed.

Our Head of IT, who leads our cybersecurity risk management and strategy processes, has over ten years of information technology and cybersecurity work experience. This risk management team member is informed about and monitors the prevention, mitigation, detection, and remediation of cybersecurity incidents through their management of, and participation in, the cybersecurity risk management and strategy processes described above, including the operation of our incident response plan.

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.

Securities Class Action Lawsuits and Derivative Actions

Two putative class action lawsuits were filed against the Company and certain of its current and former officers in the United States District Court for the Eastern District of New York, one captioned Richard S. Germond v. Spero Therapeutics, Inc., Ankit Mahadevia, and Satyavrat Shukla, Case No. 1:22-cv-03125, filed on May 26, 2022, and the other captioned Kashif Memon v. Spero Therapeutics, Inc., Ankit Mahadevia, and Satyavrat Shukla Case No. 1:22-cv-04154, filed on July 15, 2022. The parties moved to consolidate the two complaints on July 22, 2022, which were ordered consolidated on August 5, 2022 ("Consolidated Putative Class Action"). The parties filed an Amended Complaint on December 5, 2022, purported to be brought on behalf of stockholders who purchased the Company's common stock from September 8, 2020 through May 2, 2022. The Amended Complaint generally alleges that the Company and certain of its current and former officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the New Drug Application ("NDA") for tebipenem HBr in an effort to lead investors to believe that the drug would receive approval from the FDA. Plaintiffs seek unspecified damages, interest, attorneys' fees, and other costs. The Company filed a fully-briefed Motion to Dismiss on June 21, 2023. By Order entered on September 30, 2024, the Motion to Dismiss was granted, dismissing the Amended Complaint in its entirety. The Court ordered the case to be closed by Memorandum and Order entered on October 28, 2024.

A stockholder derivative action was filed against the Company, as nominal defendant, and certain of the Company's current and former officers in the United States District Court for the District of Delaware, captioned Marti v. Mahadevia, et al., Case. No. 1:23-cv-01133-RGA (the "First Derivative Complaint"), on October 11, 2023. The plaintiffs both purport to be current stockholders, and the allegations are primarily the same as those made in the Consolidated Putative Class Action. The First Derivative Complaint was transferred to the Eastern District of New York on November 13, 2023. A second stockholder derivative action was filed against the Company, as nominal defendant, and certain of its current and former officers in the Supreme Court of the State of New York, Kings County, captioned Heil v. Mahadevia, et al., Case. No. 505153/2024 (the "Second Derivative Complaint"), on February 21, 2024. The Second Derivative Complaint makes primarily the same allegations as the First Derivative Complaint, and the Consolidated Putative Class Action. The plaintiffs in both derivative suits agreed to a stay pending decision on the class action, subject to court approval. By Order entered on September 30, 2024, the motion to stay the First Derivative Complaint was denied as moot due to the dismissal of the Consolidated Putative Class Action. On March 20, 2025, the Second Derivative Complaint was voluntarily dismissed by the plaintiff.

The Company denies any allegations of wrongdoing and intends to vigorously defend against these lawsuits. However, there is no assurance that the Company will be successful in its defense or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of these actions. Moreover, the Company is unable to predict the outcomes or reasonably estimate a range of possible loss at this time.

Additional lawsuits against the Company and certain of its officers or directors may be filed in the future. If additional similar complaints are filed, absent new or different allegations that are material, the Company will not necessarily announce such additional filings.

SEC Investigation and Wells Notice

On January 9, 2025, the Company responded to a "Wells Notice" from the staff of the Boston Regional Office ("Staff") of the SEC regarding its preliminary determination to recommend a civil enforcement action or administrative proceeding against the Company, its former Chief Executive Officer and Chairman of the Board of Directors, Ankit Mahadevia, M.D. ("Dr. Mahadevia"), and its former Chief Financial Officer and President and Chief Executive Officer, Satyavrat "Sath" Shukla ("Mr. Shukla"), relating to certain public disclosures by the Company from March 31, 2022 leading up to the Company's announcement on May 3, 2022 that it had determined to cease commercialization of tebipenem HBr based on feedback from the FDA, and whether the Company's disclosures may have violated the federal securities laws (the "Investigation").

Specifically, the contemplated civil enforcement action, if approved by the Commissioners, could include allegations that the Company violated Section 17(a) of the Securities Act and Sections 10(b) and 13(a) of the Exchange Act and Rules 10b-5, 12b-20, and 13a-1 thereunder; and could allege against Dr. Mahadevia and Mr. Shukla violations of Section 17(a) of the Securities Act and Section 10(b) of the Exchange Act and Rules 10b-5 and 13a-14 thereunder. The Company, Dr. Mahadevia and Mr. Shukla continue to cooperate with the SEC, they have engaged in further dialogue with the Staff and maintain that the Company's disclosures were appropriate.

A Wells Notice is neither a formal charge of wrongdoing nor a final determination that the recipient has violated any law, but is a preliminary determination by the Staff to recommend to the SEC Commissioners that a civil enforcement action or administrative proceeding be brought against the recipients. It provides the recipients the opportunity to address in a non-public forum the issues raised by the Staff before a recommendation is made to the SEC regarding an enforcement action. If the SEC were to authorize an action against the Company and/or any of the identified individuals, it may seek an injunction or cease-and-desist order against future violations of provisions of the federal securities laws, the imposition of civil monetary penalties, disgorgement or other equitable relief within the SEC's authority, or any combination of the foregoing. The SEC could also seek an order barring each identified individual from serving as an officer or director of a public company for a specified period of time.

The results of the Investigation and the Wells Notice process and any corresponding enforcement action against the Company and/or any of the identified individuals, and the costs, timing and other potential consequences of responding and complying therewith are unknown at this time.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Our common stock is publicly traded on the Nasdaq Global Select Market under the symbol "SPRO".

Holders of Record

As of March 21, 2025, we had approximately eight 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. [Reserved]

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 clinical-stage biopharmaceutical company focused on identifying and developing novel treatments for rare diseases and diseases caused by MDR bacterial infections with high unmet need. Since our inception in 2013, we have focused our efforts and financial resources on 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 believe that our novel product candidates, if successfully developed and approved, could provide meaningful benefits to patients suffering from serious rare diseases and life-threatening bacterial infections, in both the community and hospital settings. Our pipeline consists of mid-to late-stage clinical assets.

Our most advanced clinical stage product candidate, tebipenem HBr, is in Phase 3 development, with the potential to be the first broad-spectrum oral carbapenem to treat adult patients with cUTIs, including pyelonephritis, caused by certain microorganisms. The other programs in our pipeline are SPR206 and SPR720. SPR206 is an IV-administered next generation polymyzin product candidate for the treatment of HABP/VABP caused by MDR Gram-negative bacterial infections. In March 2025, following a reprioritization of our programs, we announced that we are no longer pursuing a planned Phase 2 clinical trial for SPR206. SPR720 is a product candidate for first-line treatment of NTM pulmonary disease. In October 2024, we announced that results from a planned interim analysis of our Phase 2a clinical trial for SPR720 demonstrated the oral agent did not meet its primary endpoint and we elected to suspend development of SPR720 in its oral formulation. We are currently completing analysis of remaining data from all 25 patients dosed in the trial ahead of determining next steps.

We have experienced mostly 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, 2024, we had an accumulated deficit of $459.6 million, and cash and cash equivalents of $52.9 million. We expect to continue to incur significant expenses and operating losses for at least the next year. Based on our cash and cash equivalents as of December 31, 2024, together with earned and non-contingent development milestone payments from GSK, as well as other non-dilutive funding commitments, we believe that our cash runway will be sufficient to fund our operating expenses and required capital expenditures into the second quarter of 2026. During this period, we plan to prioritize advancing the Phase 3 clinical trial activities for tebipenem HBr under our GSK License Agreement and completing our analysis of the full dataset from the 25 treated patients in the Phase 2a proof-of-concept trial of SPR720. Beyond this point we will need additional funding, which we expect will primarily consist of raising additional capital through some combination of equity or debt financings, potential new collaborations or additional grant funding. If we are not able to secure adequate additional funding, we plan to make further reductions in spending. In that event, we may have to delay, scale back, or eliminate some or all of our planned development 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 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

Interim Leadership Changes

In January 2025, the independent directors of our Board of Directors approved the following actions as a matter of corporate governance best practices and to enable the Company to maintain focus on pursuing our business objectives pending resolution of a "Wells Notice" received from the staff of the Boston Regional Office (the "Staff") of the SEC. The Wells Notice was regarding the Staff's preliminary determination to recommend a civil enforcement action or administrative proceeding against the Company , its former Chief Executive Officer and Chairman of the Board of Directors, Ankit Mahadevia, M.D. ("Dr. Mahadevia"), and its former Chief Financial Officer and President and Chief Executive Officer, Satyavrat "Sath" Shukla ("Mr. Shukla"), relating to certain public disclosures by the Company from March 31, 2022 leading up to the announcement on May 3, 2022 that we had determined to cease commercialization of tebipenem HBr based on feedback from the FDA, and whether our disclosures may have violated the federal securities laws.

- The Board of Directors appointed director Frank Thomas to serve as the Chairman of the Board of Directors, stepping in for Ankit Mahadevia, M.D.
- Mr. Shukla agreed to a paid administrative leave from his role as President and Chief Executive Officer, pending resolution of the Investigation. During such leave, Mr. Shukla remains an employee and continues to serve as a member of the Board of Directors for the duration of his directorship term.
- The Board of Directors appointed Esther Rajavelu, our Chief Financial Officer, Chief Business Officer and Treasurer, to serve as Interim President and Chief Executive Officer during the term of Mr. Shukla's administrative leave.

The terms of Ms. Rajavelu's existing employment arrangement with the Company have been amended to provide that she will receive additional cash compensation of $20,000 per month while she serves as the Interim President and Chief Executive Officer, in addition to her role as Chief Financial Officer and Chief Business Officer.

Components of Our Results of Operations

Sales Revenue

To date, we have not generated any revenue from product sales. 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.

Grant Revenue

We expect a portion of our revenue will continue to be derived from payments under our active government awards and any awards that we may receive in the future.

Collaboration Revenue

Current collaboration revenue relates to our agreements with Pfizer and GSK.

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 ("CROs");
- costs incurred in connection with our government awards;
- the cost of consultants and contract manufacturing organizations ("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 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 any global health, economic or political crises;
- 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 our product candidates, if approved, whether alone or in collaboration with others;
- acceptance of our product candidates, if approved, by patients, the medical community and third-party payors;
- competition with other therapies; and
- a continued acceptable safety profile of our 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 we will continue to incur 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.

Restructuring

In light of our decision to suspend planned development activities for our oral SPR720 program and our strategic restructuring, we expect that our future expenses relating to development activities with respect to SPR720 will be substantially reduced as we evaluate potential paths forward for SPR720 and implement our restructuring. In connection with our restructuring, we estimate that we will incur approximately $1.1 million of costs in connection with the reduction in workforce related to severance pay and other related termination benefits of which we incurred $0.9 million during the year ended December 31, 2024 and anticipate the remaining to be incurred in 2025. We may incur additional costs not currently contemplated due to events associated with or resulting from the workforce reduction. Most of the costs associated with our workforce reduction were incurred during the quarter ended December 31, 2024.

Other Income (Expense)

Interest Income (Expense)

Interest income (expense) consists of interest income related to the significant financing component related to the GSK License Agreement and 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.

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 and vendor payables.

Income Taxes

Except for year ended December 31, 2022, 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, 2024, we had federal and state net operating loss carryforwards ("NOLs") of $165.2 million and $120.6 million, respectively which may be available to offset future income tax liabilities. $152.0 million of the federal NOLs can be carried forward indefinitely and $13.2 million of the federal NOLs begin to expire in 2034. The state NOLs begin to expire in 2034 and will expire at various dates through 2044. In addition, as of December 31, 2024, we had foreign net operating loss carryforwards of $4.6 million, which may be available to offset future income tax liabilities and do not expire. As of December 31, 2024, we also had federal and state research and development tax credit carryforwards of $6.2 million and $2.1 million, respectively, which begin to expire in 2036 and 2033, 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 (“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 collaboration arrangements. 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 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.

Revenue Recognition - GSK License Agreement

In determining the accounting treatment for the GSK License Agreement, we developed assumptions to determine the stand-alone selling price for each performance obligation in the contract. We developed the estimated standalone selling price for the license using a discounted cash flow model. To develop this model, we applied significant judgment in the determination of the significant assumptions relating to forecasted future revenues, development timelines, the discount rate, and probabilities of technical and regulatory success. We developed the estimated standalone selling price for the research and development services using a discounted cash flow model. The assumptions to develop the estimated standalone selling price for the related research and development services include estimates of costs to be incurred to fulfill its obligations associated with the performance of the research and development services, plus a reasonable margin.

When an arrangement contains payment terms that are extended beyond one year, a significant financing component may exist. We assessed our revenue-generating arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component does exist in certain arrangements. The significant financing component is calculated as the difference between the stated value and present value of the milestones payable and is recognized as interest income over the extended payment period. Judgment is used in determining: (1) whether the financing component in a license agreement is significant and, if so, (2) the discount rate used in calculating the significant financing component.

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 issue stock-based awards to employees and directors in the form of stock options and restricted stock units. We measure and recognize compensation expense for our stock-based awards granted to our employees and directors based on the estimated grant date fair value in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification Topic 718 ("ASC 718"), Compensation—Stock Compensation. We determine the fair value of restricted stock units based on the fair value of our common stock. We measure all share-based options 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. We have also granted certain awards with performance-based criteria.

Restructuring

We made estimates and judgments regarding the amount and timing of our restructuring expense and liability, including one-time termination benefits accounted for upon the announcement of our restructuring in October 2024. Restructuring charges are reflected in our consolidated statements of income.

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 recurring cash outflows from operating activities, have an accumulated deficit and need to raise additional capital to fund future operations. These factors raise substantial doubt about our ability to continue as a going concern.

Comparison of the Years Ended December 31, 2024 and 2023

The following table summarizes our results of operations for the years ended December 31, 2024 and 2023:

	Year Ended December 31,		
	2024	2023	$ Change
Revenues:			
Grant revenue	$ 20,581	$ 7,046	$ 13,535
Collaboration revenue - related party	27,025	95,802	(68,777)
Collaboration revenue	371	933	(562)
Total revenues	47,977	103,781	(55,804)
Operating expenses:			
Research and development	96,757	51,440	45,317
General and administrative	23,704	25,554	(1,850)
Restructuring	877	—	877
Impairment of long-term asset	—	5,306	(5,306)
Total operating expenses	121,338	82,300	39,038
Income (loss) from operations	(73,361)	21,481	(94,842)
Other income (expense):			
Interest income	4,735	3,937	798
Other income (expense), net	60	(14)	74
Total other income, net	4,795	3,923	872
Net income (loss) before income taxes	(68,566)	25,404	(93,970)
Income tax expense	-	(2,598)	2,598
Net income (loss)	$ (68,566)	$ 22,806	$ (91,372)

Grant Revenue

	Year Ended December 31,		
	2024	2023	$ Change
BARDA Contract (Tebipenem HBr)	$ 20,200	$ 4,361	$ 15,839
NIAID Contract (SPR206)	381	2,685	(2,304)
Total revenue	$ 20,581	$ 7,046	$ 13,535

Grant revenue recognized during 2024 and 2023 consisted of the reimbursement of qualifying expenses incurred in connection with our various government awards. The increase in revenue during 2024 was primarily due to an increase of $15.8 million in funding under our BARDA contract related to our pivotal Phase 3 clinical trial of tebipenem HBr, partially offset by a decrease of $2.3 million in qualified expenses incurred under our NIAID award relating to SPR206.

Collaboration Revenue - Related Party

During the years ended December 31, 2024 and 2023, collaboration revenue - related party related to revenue recognized under the GSK License Agreement. During the year ended December 31, 2024, we recognized $27.0 million in collaboration revenue - related party under the GSK License Agreement. During the year ended December 31, 2023, we recognized $95.8 million in collaboration revenue - related party, of which $21.2 million was recognized upon achievement of the $30.0 million milestone under the GSK License Agreement and $64.7 million upon achievement of the $95.0 million milestone under the GSK License Agreement.

Collaboration Revenue

During the year ended December 31, 2024 we recognized $0.4 million in collaboration revenue related to our agreement with Pfizer. During the year ended December 31, 2023 we recognized $0.9 million in collaboration revenue related to our agreement with Pfizer.

Research and Development Expenses

	Year Ended December 31,		
	2024	2023	$ Change
Direct research and development expenses by program:			
Tebipenem HBr	$ 60,502	$ 16,695	$ 43,807
SPR720	16,626	13,031	3,595
SPR206	570	3,240	(2,670)
Unallocated expenses:			
Personnel related (including share-based compensation)	14,111	13,788	323
Facility related and other	4,948	4,686	262
Total research and development expenses	$ 96,757	$ 51,440	$ 45,317

Direct costs related to our tebipenem HBr program increased by $43.8 million during the year ended December 31, 2024, compared to the year ended December 31, 2023, due to increased clinical activities related to our Phase 3 clinical trial of tebipenem HBr, which we initiated in the fourth quarter of 2023. Direct costs related to our tebipenem HBr program during the year ended December 31, 2024 reflect a $3.6 million reduction to expense related to a purchase of drug substance material by GSK.

Direct costs related to our SPR720 program increased by $3.6 million during the year ended December 31, 2024, compared to the year ended December 31, 2023, due to clinical activity during the period related to our Phase 2a clinical trial of SPR720, which completed enrollment in the second quarter of 2024. Subsequently, in October 2024, we announced that we would suspend current development activities for SPR720 based on an interim analysis of the Phase 2a proof-of-concept study of SPR720 for the treatment of NTM-PD not meeting its primary endpoint.

Direct costs related to our SPR206 program decreased by $2.7 million during the year ended December 31, 2024, primarily due to decreased preclinical activity.

In light of the suspension of development activities for our SPR720 program and the discontinuation of development of SPR206, we expect that direct research and development costs related to those programs will be reduced in future periods.

The increase in personnel-related costs of $0.3 million was primarily due to increased research and development personnel costs. Personnel-related costs for the years ended December 31, 2024 and 2023 included share-based compensation expenses of $2.6 million and $2.7 million, respectively.

Facility-related and other costs primarily reflect costs related to supporting our research and development staff.

General and Administrative Expenses

	Year Ended December 31,		
	2024	2023	$ Change
Personnel related (including share-based compensation)	$ 13,188	$ 15,324	$ (2,136)
Professional and consultant fees	8,198	8,151	47
Facility related and other	2,318	2,079	239
Total general and administrative expenses	$ 23,704	$ 25,554	$ (1,850)

The decrease in personnel-related costs of $2.1 million was primarily a result of decreased headcount costs in our general and administrative functions during the period. Personnel-related costs for the years ended December 31, 2024 and 2023 included share-based compensation expense of $5.2 million and $5.3 million, respectively.

The increase in professional and consultant fees was primarily due to increased legal and consulting expenses incurred during the year ended December 31, 2024.

Facility-related and other costs primarily reflect costs related to supporting our general and administrative staff.

Restructuring

During the year ended December 31, 2024, we incurred restructuring expenses of $0.9 million related to our strategic restructuring that we announced in October 2024. Restructuring expenses for the period were primarily comprised of severance and other employee costs. For further information, refer to Note 9 – Restructuring to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Impairment of Long-Term Asset

In 2023, we concluded that we have no future use for the Savior facility (further described in Note 13 – License, Collaboration and Service Agreements to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K). As such, we fully impaired this long-term asset and recorded an impairment expense of $5.3 million on the consolidated statement of operations during the year ended December 31, 2023.

Income Tax Expense

During the year ended December 31, 2023, we recorded $2.6 million of income tax expense primarily related to a change in estimate with respect to the tax treatment of the GSK License Agreement.

Other Income, Net

Other income, net was $4.8 million during 2024, compared to $3.9 million during 2023. Total other income for the year ended December 31, 2024 included $4.7 million of interest income, of which $1.5 million related to the significant financing component recognized under the GSK License Agreement, offset by immaterial fluctuations in unrealized foreign currency. Total other income for the year ended December 31, 2023 included $3.9 million of interest income, offset by fluctuations in unrealized foreign currency.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We have recognized revenue to date from funding arrangements with the DoD, NIAID, CARB-X and BARDA, the GSK License Agreement and our license agreements with Everest and Pfizer. We have not yet commercialized any of our product candidates and we may not generate revenue from sales of any product candidates. To date, we have funded our operations with payments received under license and collaboration agreements and funding from government contracts, and from the proceeds of multiple common stock offerings. As of December 31, 2024, we had cash and cash equivalents of $52.9 million.

Cash Flows

The following table summarizes our sources and uses of cash for the years ended December 31, 2024 and 2023:

	Year Ended December 31,	
	2024	2023
Cash used in operating activities	$ (23,444)	$ (32,995)
Cash provided by financing activities	—	221
Net decrease in cash and cash equivalents	$ (23,444)	$ (32,774)

Operating Activities

Net cash used in operating activities for the year ended December 31, 2024 was $23.4 million, primarily resulting from our net loss of $68.6 million, adjusted for net non-cash items of $8.8 million (primarily due to stock-based compensation). Net cash provided by changes in our operating assets and liabilities was $36.3 million and consisted primarily of a $46.4 million decrease in our related party collaboration receivable, primarily due to the receipt of the first and second installments of the development milestone payments from GSK (see Note 13 - License, Collaboration and Service Agreements), a $26.6 million net decrease in deferred revenue, offset by an increase of $17.1 million in accrued expenses and accounts payable.

Net cash used in operating activities for the year ended December 31, 2023 was $33.0 million, primarily resulting from our net income of $22.8 million, adjusted for net non-cash items of $14.6 million (primarily due to stock-based compensation and asset impairment). Net cash used by our operating assets and liabilities was $70.4 million and consisted primarily of a $95.7 million increase in our related party collaboration receivable, $29.0 million net increase in deferred revenue and a decrease of $1.7 million in accrued expenses and accounts payable.

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 programs and the timing of vendor invoicing and payments. Changes in deferred revenue are related to the GSK License Agreement and our license agreement with Pfizer. Changes in collaboration receivable - related party related to the GSK License Agreement.

Investing Activities

We did not undertake any investing activities during either of the years ended December 31, 2024 or 2023.

Financing Activities

We did not undertake any financing activities during the year ended December 31, 2024. Cash provided by financing activities during the year ended December 31, 2023 was $0.2 million, due to the $0.2 million net sales of common stock under our Sales Agreement.

Funding Requirements

Our future use of operating cash and capital requirements, and the timing and amount thereof, 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 product candidates and potential new product candidates;
- the amount of funding that we receive under government contracts that we have applied for or may apply for in the future;
- 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 our product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- 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;
- the extent to which we in-license or acquire other products and technologies; and
- costs associated with litigation and any government investigation.

As of December 31, 2024, we had cash and cash equivalents of $52.9 million. In accordance with 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 the Company's current operating plan and existing cash and cash equivalents, the Company has determined that there is substantial doubt regarding its ability to continue as a going concern within one year after the date that these consolidated financial statements are issued. Based on our cash and cash equivalents as of December 31, 2024, together with earned and non-contingent development milestone payments from GSK, as well as other non-dilutive funding commitments, we believe that our cash runway will be sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2026.

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 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. 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. If our access to capital is restricted or associated borrowing costs increase as a result of developments in financial markets, 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.

On February 25, 2025, we received a deficiency letter from the Listing Qualifications Department informing us that we were not in compliance with the continued listing requirements of the Nasdaq Global Select Market because the bid price for our common stock had closed below $1.00 per share for 30 consecutive business days. We have until August 25, 2025, to regain compliance with the bid price requirement. If we do not regain compliance with the bid price requirement, our common stock will be subject to delisting. Any potential delisting of our common stock could have a material adverse effect on the market for, and liquidity and price of, our common stock and would adversely affect our ability to raise capital on terms acceptable to us, or at all.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2024 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)	4,858	1,746	3,112	—	—
Total	$ 4,858	$ 1,746	$ 3,112	$ —	$ —

(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 $1.0 million upon the achievement of specified clinical and regulatory milestones for tebipenem HBr and (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.

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 ($6.3 million as of December 31, 2024) 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 related to SPR720 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.

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.

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, 2024, we had cash and cash equivalents of $52.9 million, consisting of cash and money market accounts. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. Treasury interest rates. We did not have any assets classified as marketable securities as of December 31, 2024. As we incur research expenses in foreign countries, we face exposure to movements in foreign currency exchange rates, primarily the Euro, British Pound and Australian dollar against the U.S. dollar. Historically, foreign currency fluctuations have not had a material impact on our consolidated financial statements.

Item 8. Financial Statements and Supplementary Data.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Spero Therapeutics, Inc. and its subsidiaries (the "Company") as of December 31, 2024 and 2023, and the related consolidated statements of operations and comprehensive loss, of 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, 2024 and 2023, 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 cash outflows from operating activities, has an accumulated deficit and needs to raise additional capital to fund future operations, which raises 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.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

External Research and Development Costs

As described in Note 2 to the consolidated financial statements, research and development costs are expensed as incurred. The Company's research and development expense for the year ended December 31, 2024 was $96.8 million, a significant portion of which relates to external research and development costs. The Company recognizes external research and development costs based on an evaluation of the progress to completion of specific tasks using information provided to the Company by its service providers. This process involves reviewing open contracts and purchase orders, communicating with applicable personnel to identify services that have been performed on the Company's behalf, and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of actual costs.

The principal consideration for our determination that performing procedures relating to external research and development costs is a critical audit matter is a high degree of auditor effort in performing procedures related to the Company's external research and development costs.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included, among others, testing external research and development costs on a sample basis, by obtaining and inspecting source documentation such as the underlying contract research organization and contract manufacturing organization agreements, purchase orders, invoices received, and information received from certain third-party service providers, where applicable.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 27, 2025

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, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 52,889	$ 76,333
Collaboration receivable, current - related party	49,391	49,152
Other receivables	3,085	1,545
Prepaid expenses and other current assets	1,911	4,178
Total current assets	107,276	131,208
Property and equipment, net	—	2
Operating lease right-of-use assets	3,114	4,155
Collaboration receivable, non-current - related party	—	46,590
Other assets	153	435
Total assets	$ 110,543	$ 182,390
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 7,306	$ 1,378
Accrued expenses and other current liabilities	17,724	6,557
Operating lease liabilities	1,746	1,718
Income taxes payable	174	387
Deferred revenue, current	368	2,132
Deferred revenue, current - related party	21,756	24,981
Total current liabilities	49,074	37,153
Non-current operating lease liabilities	2,551	3,825
Deferred revenue, non-current	12,219	10,825
Deferred revenue, non-current - related party	576	23,606
Other long-term liabilities	—	87
Total liabilities	64,420	75,496
Commitments and contingencies (Note 11)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized, no shares issued and outstanding as of December 31, 2024 and 2023	—	—
Common stock, $0.001 par value; 120,000,000 shares authorized as of December 31, 2024 and 2023; 54,593,527 shares issued and outstanding as of December 31, 2024 and 52,999,680 shares issued and outstanding as of December 31, 2023	55	53
Additional paid-in capital	505,706	497,913
Accumulated deficit	(459,638)	(391,072)
Total stockholders' equity	46,123	106,894
Total liabilities and stockholders' equity	$ 110,543	$ 182,390

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,	
	2024	2023
Revenues:		
Grant revenue	$ 20,581	$ 7,046
Collaboration revenue - related party	27,025	95,802
Collaboration revenue	371	933
Total revenues	47,977	103,781
Operating expenses:		
Research and development	96,757	51,440
General and administrative	23,704	25,554
Restructuring	877	—
Impairment of long-term asset	—	5,306
Total operating expenses	121,338	82,300
Income (loss) from operations	(73,361)	21,481
Other income (expense):		
Interest income	4,735	3,937
Other income (expense), net	60	(14)
Total other income, net	4,795	3,923
Net income (loss) before income taxes	(68,566)	25,404
Income tax expense	—	(2,598)
Net income (loss) and comprehensive income (loss)	$ (68,566)	$ 22,806
Net income (loss) per share attributable to common stockholders, basic	$ (1.27)	$ 0.43
Net income (loss) per share attributable to common stockholders, diluted	$ (1.27)	$ 0.43
Weighted average common shares outstanding, basic:	54,037,917	52,703,467
Weighted average common shares outstanding, diluted:	54,037,917	52,989,030

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

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

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Par Value			
Balances at December 31, 2022	**52,456,195**	**52**	**489,760**	**(413,878)**	**75,934**
Issuance of common stock upon the vesting of restricted stock units and performance stock units	399,009	1	—	—	1
Issuance of common stock, net of issuance costs	144,476	—	221	—	221
Share-based compensation expense	—	—	7,932	—	7,932
Net income	—	—	—	22,806	22,806
Balances at December 31, 2023	**52,999,680**	**53**	**497,913**	**(391,072)**	**106,894**
Issuance of common stock upon the vesting of restricted stock units and performance stock units	1,593,847	2	—	—	2
Share-based compensation expense	—	—	7,793	—	7,793
Net loss	—	—	—	(68,566)	(68,566)
Balances at December 31, 2024	**54,593,527**	**55**	**505,706**	**(459,638)**	**46,123**

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,	
	2024	**2023**
Cash flows from operating activities:		
Net income (loss)	$ (68,566)	$ 22,806
Adjustments to reconcile net income (loss) to net cash used in operating activities:		
Depreciation and amortization	2	367
Non-cash lease cost	1,043	969
Impairment of assets	—	5,306
Share-based compensation	7,793	7,932
Changes in operating assets and liabilities:		
Collaboration receivable, current and non-current - related party	46,351	(95,742)
Other receivables	(1,540)	(461)
Prepaid expenses and other current assets	2,267	(799)
Other assets	282	(1)
Accounts payable	5,928	761
Accrued expenses and other current liabilities	11,167	(2,416)
Deferred revenue	(370)	(933)
Deferred revenue - related party	(26,255)	29,942
Other long-term liabilities	(87)	(9)
Operating lease liabilities	(1,246)	(1,104)
Income taxes payable	(213)	387
Net cash used in operating activities	(23,444)	(32,995)
Cash flows from financing activities:		
Proceeds from the issuance of common stock, net of issuance costs	—	221
Net cash provided by financing activities	—	221
Net decrease in cash and cash equivalents	(23,444)	(32,774)
Cash and cash equivalents at beginning of period	76,333	109,107
Cash and cash equivalents at end of period	$ 52,889	$ 76,333
Supplemental disclosure of cash flow information		
Cash paid for income taxes	$ 99	$ 2,212

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

1. Nature of the Business and Basis of Presentation

The Company is a clinical-stage biopharmaceutical company focused on identifying and developing novel treatments for rare diseases and diseases caused by multi-drug resistant ("MDR") bacterial infections with high unmet need. Since the Company's inception in 2013, it has focused its efforts and financial resources on acquiring and developing product and technology rights, building our intellectual property portfolio and conducting research and development activities for its product candidates. The Company does not have any products approved for sale and has not generated any revenue from product sales. The Company believes that its novel product candidates, if successfully developed and approved, could provide meaningful benefits to patients suffering from serious rare diseases and life-threatening bacterial infections, in both the community and hospital settings. The Company's pipeline consists of mid- to late-stage clinical assets.

The Company's most advanced clinical stage product candidate, tebipenem HBr, is in Phase 3 development, with the potential to be the first broad-spectrum oral carbapenem to treat adult patients with complicated urinary tract infections ("cUTIs"), including pyelonephritis, caused by certain microorganisms. The other programs in our pipeline are SPR206 and SPR720. SPR206 is an intravenously ("IV") administered next generation polymyxin product candidate, for the treatment of hospital-acquired and ventilator-associated bacterial pneumonia ("HABP/VABP") caused by MDR Gram-negative bacterial infections. In March 2025, following a reprioritization of its programs, the Company announced that it is no longer pursuing a planned Phase 2 clinical study for SPR206. SPR720 is a product candidate for first-line treatment of nontuberculous mycobacterial ("NTM") pulmonary disease. In October 2024, the Company announced that results from a planned interim analysis of its Phase 2a clinical trial for SPR720 demonstrated the oral agent did not meet its primary endpoint, and the Company elected to suspend development of SPR720 in its oral formulation. The Company is currently completing analysis of the remaining data from all 25 patients dosed in the trial ahead of determining next steps.

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.

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 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 its collaboration and licensing agreements, funding from government contracts and through the sale of the Company's common and preferred stock. The Company has incurred recurring cash outflows from operating activities and losses in most years since its inception. During the years ended December 31, 2024 and 2023, the Company had net loss of $(68.6) million and net income of $22.8 million, respectively. In addition, as of December 31, 2024, the Company had an accumulated deficit of $459.6 million. The Company expects to continue to generate operating losses for the foreseeable future.

On February 25, 2025, the Company received a deficiency letter from the Listing Qualifications Department informing it that it was not in compliance with the continued listing requirements of the Nasdaq Global Select Market because the bid price for its common stock had closed below $1.00 per share for 30 consecutive business days. The Company has until August 25, 2025 to regain compliance with the bid price requirement. If the Company does not regain compliance with the bid price requirement, its common stock will be subject to delisting. Any potential delisting of the Company's common stock could have a material adverse effect on the market for, and liquidity and price of, the Company's common stock and would adversely affect the Company's ability to raise capital on terms acceptable to the Company, or at all.

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 and cash equivalents, the Company has determined that there is substantial doubt regarding its ability to continue as a going concern within one year after the date that these consolidated financial statements are issued. The Company will require additional funding to fund the development of its product candidates through regulatory approval and to support its continued operations. The Company will seek additional funding through public or private financings, debt financing, collaboration agreements, government grants or other venues. If our access to capital is restricted or associated borrowing costs increase as a result of developments in financial markets, 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, or product portfolio expansion 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. 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 and developing novel treatments for bacterial infections, including MDR bacterial infections, and rare diseases. All of the Company's tangible assets are held in the United States.

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, 2024, and 2023, the Company had no off-balance sheet risks, including but not limited to, 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.

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

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 sheets 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 sheets leases with terms of one year or less. As of December 31, 2024 and 2023, 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.

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 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.

Revenue Recognition – Collaboration Revenue

The Company has entered into licensing agreements that are evaluated under Accounting Standards Codification, Topic 606 ("Topic 606"), Revenue from Contracts with Customers, through which the Company licenses certain of its product candidates' rights to a third party. Terms of these arrangements include various payment types, typically including one or more of the following: upfront license fees; development, regulatory and commercial milestone payments; payments for manufacturing supply services; and/or royalties on net sales of licensed products.

Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract with a customer; (ii) identify the performance obligations under the agreement; (iii) determine the transaction price, including constraint on variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) determine how the revenue will be recognized for each performance obligation. The Company only applies the five-step model to contracts when it is probable that the Company will collect the consideration to which it is entitled in exchange for the goods or services it transfers to a customer.

Once a contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right may be accounted for as a contract modification or as a continuation of the contract for accounting purposes.

The Company assesses whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct) and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct in the evaluation of a collaboration arrangement subject to Topic 606, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, the Company is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices ("SSP") on a relative SSP basis. The SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. In certain circumstances, the Company may apply the residual method to determine the SSP of a good or service if the standalone selling price is considered highly variable or uncertain. The Company validates the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. When an arrangement contains payment terms that are extended beyond one year, a significant financing component may exist. The Company assessed its revenue-generating arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component exists in certain arrangements. The significant financing component is calculated as the difference between the stated value and present value of the milestones payable and is recognized as interest income over the extended payment period. Judgment is used in determining: (1) whether the financing component in a license agreement is significant and, if so, (2) the discount rate used in calculating the significant financing component.

For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time this is based on the use of an output or input method.

In determining the accounting treatment for these arrangements, the Company develops assumptions to determine the stand-alone selling price for each performance obligation in the contract. The Company develops the estimated standalone selling price for the license using a discounted cash flow model. To develop this model, the Company applies significant judgment in the determination of the significant assumptions relating to forecasted future revenues, development timelines, the discount rate, and probabilities of technical and regulatory success. The Company develops the estimated standalone selling price for the research and development services using a discounted cash flow model. The assumptions to develop the estimated standalone selling price for the related research and development services include estimates of costs to be incurred to fulfill its obligations associated with the performance of the research and development services, plus a reasonable margin.

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.

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.

External Research and Development 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. The Company recognizes external research and development costs based on an evaluation of the progress to completion of specific tasks using information provided to the Company by its service providers. This process involves reviewing open contracts and purchase orders, communicating with applicable personnel to identify services that have been performed on the Company's behalf, and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of actual costs. 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.

Restructuring

The Company made estimates and judgments regarding the amount and timing of its restructuring expense and liability, including one-time termination benefits and other exit costs accounted for upon the announcement of the restructuring in October 2024.

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 issues stock-based awards to employees and directors in the form of stock options and restricted stock units. The Company measures and recognizes compensation expense for its stock-based awards granted to its employees and directors based on the estimated grant date fair value in accordance with ASC 718, Compensation—Stock Compensation, and determines the fair value of restricted stock units based on the fair value of its common stock. The Company measures all share-based options 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 Income (Loss)

Comprehensive income (loss) includes net income (loss), as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2024 and 2023, there were no components of other comprehensive income (loss), and therefore comprehensive loss is the same as net loss.

Net Income (Loss) per Share

When the Company issues shares that meet the definition of participating securities, the Company follows the two-class method when computing net income (loss) per share. 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 the Company.

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.

On December 22, 2017, the Tax Cuts and Jobs Act ("TCJA") was signed into law. Under the TCJA provisions, effective with tax years beginning on or after January 1, 2022, taxpayers can no longer immediately expense qualified research and development expenditures, including all direct, indirect, overhead and software development costs. Taxpayers are now required to capitalize and amortize these costs over five years for research conducted within the United States or 15 years for research conducted abroad.

Recently Issued and Adopted Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board ("FASB") or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise noted, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its consolidated financial statements and disclosures.

In November 2024, the FASB issued an amendment to the accounting guidance on income statement presentation to require disclosure, in the notes to the financial statements, of disaggregated information about certain costs and expenses, including purchases of inventory, employee compensation, and depreciation and amortization included in each relevant expense caption within continuing operations. The guidance is effective for fiscal years beginning after December 15, 2026, and interim periods beginning after December 15, 2027. The Company is currently evaluating the impact the guidance will have on its consolidated financial statements.

In December 2023, the FASB issued ASU 2023-09, *Improvements to Income Tax Disclosures.* This ASU is related to the disclosure of rate reconciliation and income taxes paid. This guidance became effective for annual periods beginning after December 15, 2024. This standard does not have a material impact on the Company's consolidated financial statements, but it requires increased disclosures within the notes to the consolidated financial statements.

In November 2023, the FASB issued ASU 2023-07, *Improvements to Reportable Segment Disclosures.* This ASU is related to reportable segment disclosure requirements, primarily through enhanced disclosures about significant segment expenses. This guidance became effective for annual periods beginning after December 15, 2023 and interim periods beginning after December 15, 2024, and is applied on a retrospective basis. Retrospective application is required, and early adoption is permitted. The Company adopted this guidance for the year ended December 31, 2024 and applied the guidance retrospectively for all periods presented.

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, 2024 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ —	$ 52,258	$ —	$ 52,258
Total cash equivalents	—	52,258	—	52,258

	Fair Value Measurements at December 31, 2023 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ —	$ 75,628	$ —	$ 75,628
Total cash equivalents	—	75,628	—	75,628

Excluded from the tables above is cash of $0.6 million and $0.7 million as of December 31, 2024 and 2023, respectively. During the years ended December 31, 2024 and 2023, there were no transfers between Level 1, Level 2 and Level 3 categories.

4. Property and Equipment, Net

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

	December 31,	
	2024	2023
Leasehold improvements	$ 1,636	$ 1,636
Manufacturing equipment	1,338	1,338
Computer software and equipment	437	437
Office furniture and equipment	209	209
	3,620	3,620
Less: Accumulated depreciation and amortization	(3,620)	(3,618)
Total property and equipment, net	$ —	$ 2

Depreciation and amortization expense related to property and equipment was less than $0.1 million and $0.4 million for the years ended December 31, 2024 and 2023, respectively.

5. Leases

Operating Leases

The Company has entered into, and subsequently amended, an operating lease agreement with respect to its corporate headquarters located at 675 Massachusetts Avenue, Cambridge, Massachusetts where the Company leases approximately 23,400 square feet of office space. The Company's lease extends through July 2027.

For the years ended December 31, 2024 and 2023, the components of operating lease expense were as follows (in thousands):

Operating lease expense	Statement of Operations Location	December 31, 2024	December 31, 2023
Fixed operating lease expense	Research and development expense	$ 757	$ 1,048
	General and administrative expense	757	559
Variable operating lease expense	Research and development expense	35	12
	General and administrative expense	35	7
Total operating lease expense		$ 1,584	$ 1,626

Supplemental cash flow information related to the Company's operating leases for the years ended December 31, 2024 and 2023, was as follows (in thousands):

	December 31, 2024	December 31, 2023
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash flows from operating leases	$ 1,718	$ 1,690

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, 2024 and 2023 (in thousands, except for the weighted average remaining lease term and the weighted average discount rate):

Lease Assets and Liabilities	Classification	December 31, 2024	December 31, 2023
Assets			
Operating	Operating lease right-of-use assets	$ 3,114	$ 4,155
Total leased assets		$ 3,114	$ 4,155
Liabilities			
Current			
Operating	Operating lease liabilities	$ 1,746	$ 1,718
Non-Current			
Operating	Non-current operating lease liabilities	2,551	3,825
Total lease liabilities		$ 4,297	$ 5,543
Weighted average remaining lease term (in years)		2.6	3.6
Weighted average discount rate		9.8%	9.8%

The following table presents the maturity of the Company's operating lease liabilities as of December 31, 2024 (in thousands):

Years Ending December 31,	
2025	1,746
2026	1,956
2027	1,156
Total future minimum lease payments	4,858
Less imputed interest	(561)
Total operating lease liabilities	$ 4,297

6. Accrued Expenses and Other Current Liabilities

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

	December 31, 2024	December 31, 2023
Accrued payroll and related expenses	$ 5,456	$ 3,339
Accrued external research and development expenses	9,493	2,274
Accrued professional fees	2,199	708
Accrued restructuring expenses	456	—
Accrued other	120	236
Total Accrued expenses and other current liabilities	$ 17,724	$ 6,557

7. Equity

Convertible Preferred Stock

Series A, Series B, Series C, and Series D Convertible Preferred Stock

The Company previously designated 2,220 of the 10,000,000 authorized shares of preferred stock as Series A Preferred Stock, 1,000 of the 10,000,000 authorized shares of preferred stock as Series B Preferred Stock, 3,333 of the 10,000,000 authorized shares of preferred stock as Series C Preferred Stock, and 3,215,000 of the 10,000,000 authorized shares of preferred stock as Series D Preferred Stock. As of December 31, 2024, all of the Company's shares of preferred stock have been converted to common stock.

Common Stock

"At-the-Market" Offering

On March 11, 2021, the Company entered into a Controlled Equity Offering Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald & Co. ("Cantor") and filed a universal shelf registration statement on Form S-3 (Registration No. 333-254170), which became effective on March 29, 2021 (the "2021 Form S-3"), and pursuant to which the Company registered for sale up to $300.0 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 could determine, including up to $75.0 million of its common stock available for issuance pursuant to the "at-the-market" offering program under the Sales Agreement.

The 2021 Form S-3 expired on March 29, 2024. The Company filed a new universal shelf registration statement on Form S-3 with the SEC on March 15, 2024, which became effective on March 22, 2024, and pursuant to which the Company registered for sale up to $300.0 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 $75.0 million of its common stock available for issuance pursuant to the Sales Agreement.

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 of 1933, as amended (the "Securities Act"), subject to the terms of the Sales Agreement.

During the year ended December 31, 2024, the Company did not sell any shares of its common stock under the Sales Agreement. During the year ended December 31, 2023, the Company sold 144,476 shares of its common stock under the Sales Agreement at an average price of approximately $1.58 per share for aggregate gross proceeds of approximately $0.2 million prior to deducting sales commissions.

Subsequent to December 31, 2024, the Company did not sell any shares of its common stock under the Sales Agreement.

GSK License and Share Purchase Agreements

Concurrently with the execution of the GSK License Agreement, on September 21, 2022 (the "GSK Effective Date"), the Company entered into a stock purchase agreement (the "GSK SPA") with Glaxo Group Limited ("GGL"), an affiliate of GSK, which closed on November 7, 2022 (the "GSK Closing Date"), and pursuant to which GGL purchased on the GSK Closing Date 7,450,000 shares (the "GSK Shares") of the Company's common stock at a purchase price of approximately $1.20 per share, which represented a discount on the closing price of the Company's common stock on November 4, 2022, for an aggregate purchase price of $9.0 million. The GSK SPA contains certain standstill, lock-up and registration rights provisions. Upon closing, the Company recorded the fair market value of the shares issued in stockholders' equity in its condensed consolidated balance sheets.

The fair market value of 7,450,000 GSK Shares issued under the GSK SPA was $10.3 million. The GSK Shares were valued using an option pricing valuation model as the shares are subject to certain holding period restrictions. The Company accounted for the associated discount of $1.3 million as a freestanding equity-linked instrument under ASC 815. The discount was allocated as consideration for the GSK License Agreement and evaluated under ASC 606. The discount was determined not to be constrained and was included in the calculation of the total transaction price related to the GSK License Agreement as of the GSK Effective Date of the transaction. Refer to Note 14 for further discussion.

The GSK Shares were issued and sold without registration under the Securities Act in reliance on the exemptions provided by Section 4(a)(2) of the Securities Act and/or Regulation D promulgated thereunder and in reliance on similar exemptions under applicable state laws. Refer to Note 14 for further discussion.

8. Share-Based Compensation

The Company maintains two equity compensation plans, the 2017 Stock Incentive Plan, as amended (the "2017 Plan") and the 2019 Inducement Equity Incentive Plan, as amended (the "2019 Inducement Plan", and together with the 2017 Plan, the "Equity Plans"), which provide for the grant of stock-based awards to its directors, officers, consultants and other employees. The Equity Plans provide for the grant of non-qualified and incentive stock options, as well as restricted stock units ("RSUs"), restricted stock and other stock-based awards.

2017 Stock Incentive Plan

On June 28, 2017, the Company's stockholders approved 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 would be automatically increased 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 Compensation Committee of the Company's Board of Directors.

On August 17, 2021, the Company's stockholders approved amendments to the 2017 Plan. The amendments provided for the following: (i) increased the number of shares of the Company's common stock authorized for issuance under the 2017 Plan by 3,170,254 shares, (ii) removed the "evergreen" provision historically included in the 2017 Plan, and (iii) made certain other amendments.

In September 2022, the Company's stockholders approved an amendment to the 2017 Plan to increase the number of shares of the Company's common stock authorized for issuance thereunder by 2,000,000 shares.

On October 5, 2023, the Company's stockholders approved an amendment to the 2017 Plan to increase the number of shares of the Company's common stock authorized for issuance thereunder by 2,500,000 shares.

On May 29, 2024, the stockholders of the Company approved an amendment to the 2017 Plan to increase the number of shares of the Company's common stock authorized for issuance thereunder by 3,000,000 shares.

As of December 31, 2024, there were 5,707,847 shares remaining available to be issued under the 2017 Plan, as amended.

2019 Equity Incentive Plan

On March 11, 2019, the Company adopted 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 amendment to the 2019 Inducement Plan to increase the number of shares of common stock authorized for issuance thereunder by 700,000 shares. In December 2022, the Board of Directors approved an amendment to the 2019 Inducement Plan to increase the number of shares of common stock authorized for issuance thereunder by 875,000 shares.

In July 2023, the Board of Directors approved an amendment to the 2019 Inducement Plan to increase the number of shares of common stock authorized for issuance by 250,000 shares and in November 2023, the Board of Directors approved an amendment to the 2019 Inducement Plan to increase the number of shares of common stock authorized for issuance thereunder by 500,000 shares.

In March 2024, the Board of Directors approved an amendment to the 2019 Inducement Plan to increase the number of shares of common stock authorized for issuance thereunder by 500,000 shares.

As of December 31, 2024, there were 888,182 shares remaining available to be issued under the 2019 Inducement Plan, as amended.

The following table summarizes stock option activity under the Equity Plans (excluding RSUs) during the year ended December 31, 2024:

	2017 Plan	2019 Inducement Plan	Total Number of Stock Options
Outstanding as of December 31, 2023	2,569,421	296,173	2,865,594
Granted	35,604	—	35,604
Exercised	—	—	—
Forfeited or cancelled	(46,439)	(39,909)	(86,348)
Outstanding as of December 31, 2024	2,558,586	256,264	2,814,850

As of December 31, 2024, a total of 18,345,127 shares have been authorized and reserved for issuance under the Equity Plans and 6,596,029 shares were available for future issuance under such plans.

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 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,	
	2024	2023
Risk-free interest rate	3.8%	4.0%
Expected term (in years)	5.5	5.5
Expected volatility	90.2%	90.7%
Expected dividend yield	0.0%	0.0%

The following table summarizes details regarding stock options granted under the Equity Plans (excluding RSUs) for the year ended December 31, 2024:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2023	2,865,594	$ 10.89	5.76	$ 1
Granted	35,604	1.52		
Exercised	—	—		
Forfeited or cancelled	(86,348)	12.81		
Outstanding as of December 31, 2024	2,814,850	$ 10.71	4.45	$ 0
Outstanding as of December 31, 2024 - vested and expected to vest	2,814,850	$ 10.71	4.45	$ 0
Exercisable at December 31, 2024	2,667,152	$ 10.60	4.33	$ 0

The weighted average grant-date fair value of stock options granted during the year ended December 31, 2024 was $1.12 per share. The weighted average grant-date fair value of awards granted during the year ended December 31, 2023 was $1.29 per share. No stock options were exercised during both the years ended December 31, 2024 and 2023. The Company satisfies stock option exercises with newly issued shares of its common stock.

As of December 31, 2024, total unrecognized compensation cost related to unvested stock option grants was approximately $1.1 million. This amount is expected to be recognized over a weighted average period of less than one year.

Restricted Stock Units

The following table summarizes RSU activity under the Equity Plans (excluding performance-based RSUs) during the year ended December 31, 2024:

	Number of RSU Shares	Weighted Average Grant Date Fair Value
Outstanding as of December 31, 2023	5,368,807	$ 2.45
Granted	3,638,496	1.54
Vested and released	(1,523,848)	2.72
Forfeited or cancelled	(1,444,723)	1.88
Outstanding as of December 31, 2024	6,038,732	$ 1.97

As of December 31, 2024, there was approximately $8.5 million of total unrecognized compensation expense related to RSUs, which is expected to be recognized over a weighted-average period of approximately 2.5 years.

The fair value of the RSUs is determined on the date of grant based on the market price of the Company's common stock on that date. Each RSU represents the right to receive one share of the Company's common stock, upon vesting. Other than RSUs granted as retention awards, the RSUs vest in four equal annual installments, subject to the individual's continued service to the Company through the applicable vesting date, and are subject to the terms and conditions of the Company's form of RSU agreement under the 2017 Plan and 2019 Inducement Plan, as applicable.

Performance-Based Awards

In September 2022, the Company approved an award of 140,000 performance-based stock units as part of an executive inducement grant (the "Inducement PSUs"). The Inducement PSUs were awarded based on certain performance criteria relating to pipeline execution, business development, and financial stewardship. As these performance criteria were deemed to be achieved by May 31, 2023, 70,001 of the Inducement PSUs vested in September 2023 and the remaining 69,999 of the Inducement PSUs vested in September 2024 upon fulfillment of the service condition.

The following table summarizes Inducement PSU activity under the Equity Plans during the year ended December 31, 2024:

	Number of Performance Based Option Shares	Weighted Average Grant Date Fair Value
Outstanding as of December 31, 2023	69,999	1.08
Granted	—	—
Vested and released	(69,999)	1.08
Forfeited or cancelled	—	—
Outstanding as of December 31, 2024	—	—

Share-Based Compensation Expense

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

	Year Ended December 31,	
	2024	2023
Research and development expenses	$ 2,605	$ 2,654
General and administrative expenses	5,188	5,278
Total	$ 7,793	$ 7,932

9. Restructuring

On October 29, 2024, the Company implemented a strategic restructuring initiative and corresponding reduction in workforce. The Company restructured its operations to reduce costs and reallocate resources in support of the development of tebipenem HBr and other corporate activities. The restructuring reduced the Company's workforce by 27% from the headcount as of September 30, 2024.

The following tables summarize the restructuring related charges by line item within the Company's consolidated statements of operations where they were recorded during the year ended December 31, 2024:

	Year Ended December 31, 2024		
	Research and development	General and administrative	Total
Severance and other employee costs	$ 660	$ 217	$ 877
Total restructuring charges	$ 660	$ 217	$ 877

The Company did not recognize any restructuring charges during the year ended December 31, 2023.

The restructuring charge was included in accrued expenses and other current liabilities in the Company's consolidated balance sheets as of December 31, 2024. Activity for the period is summarized as follows (amounts in thousands):

	As of December 31, 2024
Balance as of December 31, 2023	$ —
Charge to expense	877
Payments made	(421)
Balance as of December 31, 2024	$ 456

The estimated charges that the Company expects to incur as a result of the restructuring are subject to several assumptions, and actual results may differ materially from these estimates.

Retention Awards

In connection with the restructuring, on October 29, 2024, the Board of Directors approved retention awards for non-executive employees of the Company. Subject to remaining actively employed and in good standing with the Company, aggregate retention awards of $4.4 million will be paid as a cash bonus with one half payable upon the achievement of each of two clinical execution milestones related to facilitating the clinical progress of the PIVOT-PO trial for tebipenem HBr. The awards contain certain clawback provisions in the event an employee voluntarily terminates his or her employment prior to the achievement of the second clinical execution milestone. Expenses related to these retention awards are being recognized over the employee service period from October 29, 2024 to the fourth quarter of 2025.

Executive Retention Awards

On November 8, 2024, the Compensation Committee of the Board of Directors approved a retention program for the Company's executive leadership team ("ELT"), which consists of four executive officers, including the Chief Executive Officer, Chief Financial and Chief Business Officer, Chief Operating Officer and Chief Human Resources Officer. The purpose of the program is to ensure that the Company retains ELT members who are considered critical to the development of tebipenem HBr in its ongoing PIVOT-PO, global Phase 3 clinical trial of tebipenem HBr in patients with cUTI. The retention program provides these ELT members with the opportunity to earn a cash bonus in an amount equaling 75% of the aggregate of their current base salary plus target annual bonus upon achievement of certain performance milestones related to facilitating the progress of PIVOT-PO and certain goals related to the Company's stock price appreciation or financial stewardship. Specifically, one-third of the retention payout is payable upon the achievement of each of two clinical execution milestones. The remaining one-third is payable upon the achievement of the stock price appreciation or financial stewardship milestone by no later than the fourth quarter of 2026. If fully achieved, the total retention payments would aggregate to $2.1 million. The program contains certain clawback provisions in the event an executive voluntarily terminates his or her employment prior to the achievement of the second clinical execution milestone. The program also provides for full payment in the event of certain change in control transactions. If the Company terminates an executive's employment, prior to the end of the performance period, other than for cause, then such executive will be entitled to payment of the clinical execution milestone payments. In the event that the Company's collaboration partner materially alters the PIVOT-PO work plan with the effect of preventing or indefinitely delaying the achievement of the clinical execution milestones, then the clinical execution milestone payments will be accelerated and paid in full. Expenses related to the achievement of each of the two clinical milestones are being recognized over the employee service period from October 29, 2024 to the fourth quarter of 2025. Expenses related to the achievement of the Company's stock price appreciation or financial stewardship milestone will be recognized over an employee service period starting when achievement is deemed probable but not later than the fourth quarter of 2026.

10. Income Taxes

The Company's provision for income taxes is comprised of the following for the periods ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,	
	2024	2023
Current:		
Federal	$ —	$ 2,488
State	—	110
Foreign	—	—
	—	2,598
Deferred:		
Federal	—	—
State	—	—
Foreign	—	—
	—	—
Provision for income taxes	$ —	$ 2,598

The Company recorded $2.6 million of income tax expense in 2023 related to a change in estimate with respect to the tax treatment of the GSK License Agreement, which resulted in taxable income and the utilization of $236.5 million of U.S. federal net operating losses and $6.9 million of U.S. federal research and development tax credits on its amended 2022 U.S. federal tax return.

During the years ended December 31, 2024 and 2023, the Company recorded no income tax benefits for the net operating income (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 income (loss) before income taxes were as follows (in thousands):

	Year Ended December 31,	
	2024	2023
Domestic	$ (68,566)	$ 25,404
Foreign	-	-
Income (loss) before income taxes	$ (68,566)	$ 25,404

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,	
	2024	2023
Federal statutory income tax rate	(21.0)	21.0
Federal tax credits	(4.3)	(4.9)
State taxes, net of federal benefit	1.6	(0.4)
Nondeductible stock compensation	0.8	8.5
Other nondeductible items	-	0.3
Other	(1.0)	(1.0)
Reduction in tax attributes	-	13.9
Increase in deferred tax asset valuation allowance	21.0	(27.2)
Deferred true-up	2.9	-
Effective income tax rate	— %	10.20

Net deferred tax assets as of December 31, 2024 and 2023 consisted of the following (in thousands):

	December 31,	
	2024	2023
Net operating loss carryforwards	$ 42,310	$ 25,646
Deferred revenue	41,745	47,014
Research and development and orphan drug tax credit carryforwards	10,952	7,612
Capitalized research and development expenses	21,149	21,342
Other	6,101	6,264
Total deferred tax assets	122,257	107,878
Valuation allowance	(122,257)	(107,878)
Net deferred tax assets	$ —	$ —

As of December 31, 2024, the company had United States federal, state and foreign net operating loss carryforwards ("NOLs") of $165.2 million, $120.6 million and $4.6 million, respectively. $152 million federal NOLs can be carried forward indefinitely and $13.2 million of NOLs begin to expire in 2034. The state NOLs begin to expire in 2034 and will expire at various dates through 2044. The foreign NOLs do not expire. As of December 31, 2024, the Company also had federal and state research and development tax credit carryforwards of $6.2 million and $2.1 million respectively, and federal orphan drug tax credit carryforwards of $2.9 million, which may be available to offset future income tax liabilities. The federal and state research and development tax credits begin to expire in 2036 and 2033, respectively, and the federal orphan drug credits begin to expire in 2044.

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. If the Company experiences 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. The Company recently completed a Section 382 study and concluded that we underwent several ownership changes as defined by the Code, the last of which occurred during the year ended December 31, 2018. Any carryforwards that will expire prior to utilization were removed from deferred tax assets, with a corresponding reduction of the valuation allowance. Future ownership changes may limit our ability to utilize remaining tax attributes.

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, 2024 and 2023. 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, 2024 and 2023 related primarily to the increase in net operating loss carryforwards and research and development tax credit carryforwards partially offset by a reduction in deferred revenue, and were as follows (in thousands):

	December 31,	
	2024	2023
Valuation allowance as of beginning of year	$ (107,878)	$ (114,790)
Increases recorded to income tax provision	(14,379)	6,912
Valuation allowance as of end of year	$ (122,257)	$ (107,878)

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2024 or 2023. 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, 2024 or 2023, 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 conducted a study of its research and development (R&D) credit carryforwards for the years 2016 to 2023. We have updated the carryforwards for the result of the study and the changes were not material.

The Company had filed separate U.S. income tax returns return for each of its subsidiaries prior to its reorganization in 2015. The Company now files 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 tax years 2021 and forward. 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.

11. Commitments and Contingencies

As a public biotechnology company, the Company operates in a regulated environment, and from time to time, is party to various legal proceedings and receives regulatory inquiries arising in the ordinary course of business. The costs and outcome of litigation, regulatory, investigatory or other proceedings cannot be predicted with certainty, and some lawsuits, claims, actions or proceedings may be disposed of unfavorably to the Company and could have a material adverse effect on the Company's results of operations or financial condition. In addition, intellectual property disputes often have a risk of injunctive relief which, if imposed against the Company, could materially and adversely affect its financial condition or results of operations. If a matter is both probable to result in a material liability and the amount of loss can be reasonably estimated, the Company accrues the estimated loss. Disclosure is provided when a loss is considered probable, but the loss is not reasonably estimable and when a material loss is reasonably possible but not probable. If such a loss is not probable or cannot be reasonably estimated, a liability is not recorded. As of December 31, 2024 and 2023, no material accruals have been recorded for potential contingencies related to these matters.

License Agreements

The Company has entered into license agreements with various parties under which it is obligated to make contingent and non-contingent payments (see Note 13).

Operating Leases

The Company has entered into an operating lease agreement 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 and its officers 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 executive officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. The process surrounding the Investigation and the Wells Notice (both as defined below) has resulted in legal expenses and certain liabilities for the Company and the named individuals, and each of the named individuals, as directors and officers of the Company, are entitled to indemnification for certain costs associated with the Investigation and the Wells Notice. The Company maintains a general liability insurance policy that covers certain expenses and liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers (the "D&O Insurance"), however, the total expenses and liabilities in connection with the Investigation and the Wells Notice and the amount that will be covered by such D&O Insurance is unknown at this time.

Legal Proceedings

Securities Class Action Lawsuits and Derivative Actions

Two putative class action lawsuits were filed against the Company and certain of its current and former officers in the United States District Court for the Eastern District of New York, one captioned Richard S. Germond v. Spero Therapeutics, Inc., Ankit Mahadevia, and Satyavrat Shukla, Case No. 1:22-cv-03125, filed on May 26, 2022, and the other captioned Kashif Memon v. Spero

Therapeutics, Inc., Ankit Mahadevia, and Satyavrat Shukla Case No. 1:22-cv-04154, filed on July 15, 2022. The parties moved to consolidate the two complaints on July 22, 2022, which were ordered consolidated on August 5, 2022 ("Consolidated Putative Class Action"). The parties filed an Amended Complaint on December 5, 2022, purported to be brought on behalf of stockholders who purchased our common stock from September 8, 2020 through May 2, 2022. The Amended Complaint generally alleges that the Company and certain of its current and former officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the New Drug Application ("NDA") for tebipenem HBr in an effort to lead investors to believe that the drug would receive approval from the FDA. Plaintiffs seek unspecified damages, interest, attorneys' fees, and other costs. The Company filed a fully-briefed Motion to Dismiss on June 21, 2023. By Order entered on September 30, 2024, the Motion to Dismiss was granted, dismissing the Amended Complaint in its entirety. The Court ordered the case to be closed by Memorandum and Order entered on October 28, 2024.

A stockholder derivative action was filed against the Company, as nominal defendant, and certain of the Company's current and former officers in the United States District Court for the District of Delaware, captioned Marti v. Mahadevia, et al., Case. No. 1:23-cv-01133-RGA (the "First Derivative Complaint"), on October 11, 2023. The plaintiffs both purport to be current stockholders, and the allegations are primarily the same as those made in the Consolidated Putative Class Action. The First Derivative Complaint was transferred to the Eastern District of New York on November 13, 2023. A second stockholder derivative action was filed against the Company, as nominal defendant, and certain of its current and former officers in the Supreme Court of the State of New York, Kings County, captioned Heil v. Mahadevia, et al., Case. No. 505153/2024 (the "Second Derivative Complaint"), on February 21, 2024. The Second Derivative Complaint makes primarily the same allegations as the First Derivative Complaint, and the Consolidated Putative Class Action. The plaintiffs in both derivative suits agreed to a stay pending decision on the class action, subject to court approval. By Order entered on September 30, 2024, the motion to stay the First Derivative Complaint was denied as moot due to the dismissal of the Consolidated Putative Class Action. On March 20, 2025, the Second Derivative Complaint was voluntarily dismissed by the plaintiff.

The Company denies any allegations of wrongdoing and intends to vigorously defend against these lawsuits. However, there is no assurance that the Company will be successful in its defense or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of these actions. Moreover, the Company is unable to predict the outcomes or reasonably estimate a range of possible loss at this time.

Additional lawsuits against the Company and certain of its officers or directors may be filed in the future. If additional similar complaints are filed, absent new or different allegations that are material, the Company will not necessarily announce such additional filings.

SEC Investigation and Wells Notice

On January 9, 2025, the Company responded to a "Wells Notice" from the staff of the Boston Regional Office ("Staff") of the SEC regarding its preliminary determination to recommend a civil enforcement action or administrative proceeding against the Company, its former Chief Executive Officer and Chairman of the Board of Directors, Ankit Mahadevia, M.D. ("Dr. Mahadevia"), and its former Chief Financial Officer and President and Chief Executive Officer, Satyavrat "Sath" Shukla ("Mr. Shukla"), relating to certain public disclosures by the Company from March 31, 2022 leading up to the Company's announcement on May 3, 2022 that it had determined to cease commercialization of tebipenem HBr based on feedback from the U.S. Food and Drug Administration, and whether the Company's disclosures may have violated the federal securities laws (the "Investigation").

Specifically, the contemplated civil enforcement action, if approved by the SEC Commissioners, could include allegations that the Company violated Section 17(a) of the Securities Act and Sections 10(b) and 13(a) of the Exchange Act and Rules 10b-5, 12b-20, and 13a-1 thereunder; and could allege against Dr. Mahadevia and Mr. Shukla violations of Section 17(a) of the Securities Act and Section 10(b) of the Exchange Act and Rules 10b-5 and 13a-14 thereunder. The Company, Dr. Mahadevia and Mr. Shukla continue to cooperate with the SEC, they have engaged in further dialogue with the staff and maintain that the Company's disclosures were appropriate.

A Wells Notice is neither a formal charge of wrongdoing nor a final determination that the recipient has violated any law, but is a preliminary determination by the Staff to recommend to the SEC Commissioners that a civil enforcement action or administrative proceeding be brought against the recipients. It provides the recipients the opportunity to address in a non-public forum the issues raised by the Staff before a recommendation is made to the SEC regarding an enforcement action. If the SEC were to authorize an action against the Company and/or any of the identified individuals, it may seek an injunction or cease-and-desist order against future violations of provisions of the federal securities laws, the imposition of civil monetary penalties, disgorgement or other equitable relief.

12. 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 cUTI caused by antibiotic resistant Gram-negative bacteria and for assessment against biodefense pathogens. The original 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.

As of December 31, 2024, through a number of contract modifications and the exercise of additional contract options by BARDA, including an additional contract modification of $11.7 million executed in July 2024, the committed funding increased to $59.3 million and the period of performance extended through December 31, 2025.

During the years ended December 31, 2024 and 2023, the Company recognized $20.2 million and $4.4 million of grant revenue under the BARDA agreement, respectively.

As of December 31, 2024, of the $59.3 million of committed funding, the Company has cumulatively recognized $56.7 million of grant revenue under the BARDA agreement.

Biodefense Study Option

As of December 31, 2024, uncommitted funding of $12.7 million is outstanding under the award. This uncommitted funding is exercisable by BARDA, subject to the availability of funding as well as progress and results from biodefense studies, if initiated, as part of an inter-agency collaboration between BARDA and the Defense Threat Reduction Agency.

NIAID

In May 2021, the Company was awarded a five-year contract from the U.S. National Institute of Allergy and Infectious Diseases ("NIAID") under the Agency's Omnibus Broad Agency Announcement No. HHS-NIH-NIAID-BAA2020-1 award mechanism to support further development of SPR206. Funding will be used to offset certain expenses related to manufacturing, clinical, non-clinical and regulatory activities. The Company can receive up to $27.0 million over a base period and six option periods, including an additional contract modification of $3.4 million executed in August 2024 for SPR206 Phase 2 start up activities under Option 1 of the NIAID agreement. As of December 31, 2024, $10.5 million of funding has been committed under this award.

The Company recognized $0.4 million and $2.7 million of grant revenue under this agreement during the years ended December 31, 2024 and 2023, respectively.

As of December 31, 2024, of the $10.5 million of committed funding, the Company has cumulatively recognized $5.3 million of grant revenue under the NIAD agreement.

13. 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.

Tebipenem HBr Agreements

GSK License Agreement

On November 7, 2022, the Company closed the transactions contemplated by the GSK License Agreement, which was entered into on September 21, 2022. Pursuant to the terms of the GSK License Agreement, the Company granted GSK an exclusive royalty-bearing license, with the right to grant sublicenses, under the Company's intellectual property and regulatory documents and a sublicense under certain intellectual property of Meiji Seika Pharma Co. Ltd. ("Meiji") and Meiji's regulatory documents to develop,

manufacture and commercialize tebipenem pivoxil and tebipenem HBr and products that contain tebipenem pivoxil and tebipenem HBr (the "GSK Licensed Products") in all territories, except certain Asian countries previously licensed to Meiji (Japan, Bangladesh, Brunei, Cambodia, China, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, South Korea, Taiwan, Thailand and Vietnam (the "Meiji Territory")) (the "GSK Territory"). If the Company's license with Meiji is terminated, or if Meiji forfeits or loses its rights to develop, manufacture and commercialize tebipenem HBr and products that contain tebipenem HBr in any countries in the Meiji Territory, then GSK will have an exclusive first right to negotiate with the Company to add any such countries to the GSK Territory.

Under the terms of the GSK License Agreement, in November 2022, the Company received an upfront payment of $66.0 million for GSK to secure rights to the medicine.

In July 2023, the Company received written agreement from the FDA, under a special protocol assessment ("SPA"), on the design and size of PIVOT-PO, a pivotal Phase 3 clinical trial of tebipenem HBr in patients with cUTI, including acute pyelonephritis. Under the terms of the GSK License Agreement, the Company received a $30.0 million development milestone payment during the third quarter of 2023.

In December 2023, the Company commenced enrollment in PIVOT-PO with its first patient, first visit. Under the terms of the GSK License Agreement, the Company is entitled to receive a $95.0 million development milestone that is payable in four equal semiannual installments. The Company received the first installment payment of $23.8 million for such development milestone in February 2024, the second installment payment of $23.8 million in August 2024 and the third installment payment in February 2025. The Company expects to receive the final payment of $23.8 million in the third quarter of 2025.

Remaining potential payments under the GSK License Agreement are milestone and royalty based, and are as follows (in millions):

Event	Milestone payments (up to)
GSK's submission of a new drug application with the FDA for tebipenem HBr	$25.0
Total potential commercial milestone payments based on first sale (US/EU)	$150.0
Total potential sales milestone payments	$225.0
Royalties	Low-single digit to low-double digit (if sales exceed $1.0 billion) tiered royalties on net product sales

Amendments to the GSK License Agreement

In July 2023, the Company entered into Amendment 1 to the GSK License Agreement, which updated the timeframe for technology transfer in the GSK License Agreement.

In December 2023, the Company entered into Amendment 2 to the GSK License Agreement, which added a country to the locations for PIVOT-PO enrollment. Under the terms of Amendment 2, the Company may receive up to an additional $4.3 million in milestones based on activities in such country. The Company received the first milestone payment under Amendment 2 of $1.2 million in August 2024 and received the second milestone payment of $1.3 million in October 2024. The third milestone was achieved in December 2024 and payment of the $0.7 million milestone was received in February 2025.

In March 2024, the Company entered into Amendment 3 to the GSK License Agreement, which assigns its rights to Product Trademarks (as defined in Amendment 3 to the GSK License Agreement) to GSK.

In October 2024, the Company entered into Amendment 4 to the GSK License Agreement, under which the Company will receive an additional $0.8 million upon completion of activities related to an additional Phase 1 clinical study. The Company received $0.4 million of the milestone in January 2025 and anticipates receipt of the remaining milestone in the second quarter of 2025.

Royalties are subject to reduction in the event of third-party licenses, entry of a generic product or expiration of patent and regulatory exclusivity prior to the tenth anniversary of the first commercial sale of a GSK Licensed Product in a particular country.

The Company is responsible for the execution and costs of the follow-up Phase 3 clinical trial of tebipenem HBr. GSK will be responsible for the execution and costs of any additional further development, including additional Phase 3 regulatory filing and

commercialization activities for tebipenem HBr in the GSK Territory. The Company is also responsible for providing and paying for the clinical supply of tebipenem HBr while GSK will be responsible for the costs of the commercial supply of tebipenem HBr. A joint development committee has been established between GSK and the Company to coordinate and review development activities for tebipenem HBr in the United States.

Unless earlier terminated due to certain material breaches of the GSK License Agreement or by GSK for convenience, or otherwise, the GSK License Agreement will expire on a jurisdiction-by-jurisdiction and GSK Licensed Product-by-GSK Licensed Product basis on the latest to occur of (i) loss of patent exclusivity, (ii) loss of regulatory exclusivity or (iii) ten years following the date of the first commercial sale of such licensed product in such country (the "GSK Royalty Term"). During the GSK Royalty Term, the Company has agreed not to develop, manufacture or commercialize any oral carbapenem for any indication or any oral antibiotic for cUTI; this restriction does not apply to any third party which acquires control of the Company after the date of the GSK License Agreement if certain conditions are met.

The Company has the right to terminate the GSK License Agreement upon a material breach by, or bankruptcy of, GSK. GSK has the right to terminate the GSK License Agreement at any time upon a specified number of days' notice or upon a material breach by, or bankruptcy of, the Company. In addition, in the event that GSK has the right to terminate the GSK License Agreement due to a material breach by the Company, GSK may elect not to terminate the GSK License Agreement and in lieu thereof may assume the responsibility and expense of development of tebipenem HBr in the United States, in which event GSK's obligation to make further development payments to the Company (including unpaid installments of any earned milestone payments) would cease, and/or to reduce all subsequent commercial and sales milestone payments and royalty payments otherwise due by GSK to the Company under the GSK License Agreement by 50%. In the case of a Change of Control of Spero, GSK similarly may, in lieu of terminating the GSK License Agreement, assume responsibility and expense of development of tebipenem HBr in the United States and no development milestones would be payable to the Company, as described above.

The GSK License Agreement contains representations and warranties, other covenants, indemnification provisions and other terms and conditions customary for transactions of the type contemplated by the GSK License Agreement. In support of certain of its rights to indemnification, GSK also has certain rights to suspend payments otherwise owed to the Company, as well as the right to offset payments otherwise owed to the Company against certain indemnifiable claims.

Accounting Analysis and Revenue Recognition

The Company determined that GSK is a customer and that the GSK License Agreement is within the scope of ASC 606 as licensing intellectual property and performing ongoing research and development services are ordinary activities that are ongoing and central to the Company's operations. 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 standalone selling prices ("SSP"); and (v) recognized revenue when each performance obligation was deemed to be satisfied.

Based on that evaluation, the Company identified two performance obligations, related to the license and to research and development services.

The Company developed the estimated SSP for the license using a discounted cash flow model. In developing this estimate, the Company applied significant judgment in the determination of the significant assumptions relating to forecasted future cash flows, the discount rate, and the probability of success. The SSP for the research and development services was estimated based on the Company's estimate of costs to be incurred to fulfill its obligations associated with the performance of the research and development services, plus a reasonable margin.

At contract inception, the total transaction price was $64.7 million, which included the initial payment of $66.0 million in the fourth quarter of 2022 and the discount of $1.3 million related to the stock purchase agreement ("GSK SPA") with Glaxo Group Limited, an affiliate of GSK (see Note 7). At contract inception, $45.7 million of the initial $64.7 million was allocated to the license transfer performance obligation, which was fully satisfied and recognized as revenue upon delivery of the license. The remaining $19.0 million was allocated to the research and development services obligation and is being recognized over time as services are delivered, estimated to be over a three-year period.

The Company recognized revenue for the license performance obligation at a point in time, that is upon transfer of the license to GSK. Control of the license was transferred on September 21, 2022 (the "GSK Effective Date") and GSK could begin to use and benefit from the license at the GSK Effective Date.

The $30.0 million milestone payment received by the Company under the GSK License Agreement was accounted for as variable consideration under ASC 606 and was added to the transaction price in the third quarter of 2023. Of this $30.0 million milestone, $21.2 million was recognized upon achievement of the milestone and the remaining $8.8 million was allocated to the research and development services performance obligation and will be recognized over time as the services are delivered, on a cumulative catch-up basis.

The Company is entitled to receive the $95.0 million milestone payment in four equal semiannual installments under the GSK License Agreement. This milestone was accounted for as variable consideration under ASC 606 and was added to the transaction price in the fourth quarter of 2023. The Company determined that a significant financing component of $2.5 million exists related to extended payments terms granted to GSK. The Company presents the effects of the financing component separately from collaboration revenue – related party as a component of interest income in its consolidated statement of operations. Of the $95.0 million milestone, $64.7 million was recognized upon achievement of the milestone in the fourth quarter of 2023, and the remaining amount after the $2.5 million significant financing component was allocated to the research and development services performance obligation and will be recognized over time as the services are delivered, on a cumulative catch-up basis.

The milestone installment payments are classified as collaboration receivable – related party on the Company's consolidated balance sheet as of December 31, 2024. The Company received the first installment payment of $23.8 million during the first quarter of 2024, received the second installment payment of $23.8 million in the third quarter of 2024 and received the third installment payment of $23.8 million in the first quarter of 2025. The final payment of $23.8 million is due in the third quarter of 2025.

The potential future development milestone payments from the GSK License Agreement will be accounted for as variable consideration under ASC 606. Given the uncertain nature of these payments, the Company determined they were fully constrained as of December 31, 2024 and not included in the transaction price. The Company can also earn sales-based royalties.

Pursuant to Amendment 2 to the GSK License Agreement, the Company allocated $3.2 million of the total potential additional milestones of $4.3 million to the research and development services obligation, as those development milestones were considered probable of achievement. These potential milestones were accounted for as variable consideration under ASC 606 and were added to the transaction price in the fourth quarter of 2023 and will be recognized over time as services are delivered. When and if the remaining $1.1 million milestone is deemed probable of being achieved, it will be added to the transaction price and will be recognized over time as services are delivered.

Pursuant to Amendment 4 to the GSK License Agreement, the Company allocated $0.8 million of the total potential additional milestones to the research and development services obligation, as those development milestones were considered probable of achievement. These potential milestones were accounted for as variable consideration under ASC 606 and were added to the transaction price in the fourth quarter of 2024 and will be recognized over time as services are delivered.

In total and inclusive of the above, the Company recognized $27.0 million and $95.8 million during the years ended December 31, 2024 and 2023, respectively, related to the performance obligations, which were recorded as collaboration revenue – related party on its consolidated statement of operations.

The remaining transaction price balance of approximately $22.3 million from the GSK License Agreement allocated to the research and development services performance obligation has been recorded as deferred revenue – related party in the consolidated balance sheets. As of December 31, 2024, the research and development services related to the performance obligations are expected to be recognized as costs are incurred over the project development timeframe.

Meiji License Agreement

In June 2017, the Company entered into agreements with Meiji, whereby Meiji granted to the Company a license under certain patents, know-how and regulatory documentation to research, develop, manufacture and sell products containing a proprietary compound in the licensed territory. In exchange for the 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. 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 sheets as of December 31, 2024. In October 2021, the Company paid a $1.0 million milestone payment to Meiji upon submission of an NDA to the FDA for tebipenem HBr.

The Company was obligated to pay Meiji a low double-digit percentage of any sublicense fees received by the Company up to a maximum amount of $7.5 million, of which the Company paid $6.6 million during the year ended December 31, 2022 and paid the remaining $0.9 million in the fourth quarter of 2023. The Company recorded these amounts as research and development expenses in the Company's consolidated statement of operations.

The Company is obligated to make future milestone payments of up to $1.0 million upon the achievement of specified regulatory milestones and 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.

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 reasons, and (ii) under certain circumstances arising out of the head license with a global pharmaceutical company.

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 was classified as a prepaid asset on the Company's consolidated balance sheets and was fully amortized as of December 31, 2021. The Company paid Savior an additional $5.3 million for facility build out costs between 2019 and 2021. In the third quarter of 2023, the Company concluded that it had no future use for the Savior facility and in October 2023, the Company terminated the service agreement. As such, the Company fully impaired this long-term asset and recorded an impairment expense of $5.3 million on its consolidated statement of operations during the year ended December 31, 2023.

SPR720 Agreements

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, the Company 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 years ended December 31, 2024 and 2023, the Company did not record any research and development expense under this agreement and the next milestone under this agreement is not accrued because it is not yet probable.

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.

SPR206 Agreements

Cantab License Agreement

In June 2016, the Company entered into a stock purchase agreement (the "Cantab Agreement") with Pro Bono Bio PLC, a corporation organized under the laws of England, and its affiliates, including PBB Distributions Limited ("PBB"), Cantab Anti-Infectives Ltd. and New Pharma License Holdings Limited. Under the Cantab Agreement, the Company is obligated to make future milestone payments of up to $5.8 million upon the achievement of specified clinical and regulatory milestones and a payment of £5.0 million ($6.3 million as of December 31, 2024) upon the achievement of a specified commercial milestone. In addition, the Company 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 both the years ended December 31, 2024 and 2023, the Company did not record any research and development expense related to the achievement of regulatory milestones for SPR206, as no milestones were met or are probable of being met as of the balance sheet date.

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.

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 ("Everest"). 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 "Everest Licensed Products"), in Greater China (which includes Mainland China, Hong Kong and Macau), South Korea and certain Southeast Asian countries (the "Everest Territory"). The Company retained development, manufacturing and commercialization rights with respect to SPR206 and Everest Licensed Products in the rest of the world and also retained the right to develop or manufacture SPR206 and Everest Licensed Products in the Everest Territory for use outside the Everest 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 Everest Territory.

On January 15, 2021, the Company entered into an amended and restated license agreement ("the Amended Everest License Agreement") with Everest and Spero Potentiator, Inc., 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 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 Everest Territory 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 Everest Licensed Products in the Everest Territory following regulatory approval of SPR206. Everest has the right to sublicense to affiliates and third parties in the Everest Territory.

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

To date, all performance obligations under the contract were fully satisfied.

As of December 31, 2024 remaining future milestone payments of $34.0 million are fully constrained, and will be recognized when and if achievement of those milestones becomes probable.

During both the years ended December 31, 2024 and 2023, the Company did not recognize revenue under this agreement.

Pfizer License and Share Purchase Agreements

On June 30, 2021, the Company and Pfizer Inc. ("Pfizer") entered into the Pfizer License Agreement and the Pfizer Purchase Agreement. Under the terms of the Pfizer License Agreement, the Company granted Pfizer an exclusive royalty-bearing license to develop, manufacture and commercialize SPR206 or products that contain SPR206 (the "Pfizer Licensed Products") globally with some territorial exceptions (the "Pfizer Territory"). The Pfizer Territory excludes the United States and the Asian markets previously licensed to Everest, those being the People's Republic of China, including Hainan Island, the Hong Kong Special Administrative Region of the People's Republic of China, and the Macau Special Administrative Region of the People's Republic of China, Taiwan, the Republic of Korea (South Korea), the Republic of Singapore, Malaysian Federation, Kingdom of Thailand, the Republic of Indonesia, Socialist Republic of Vietnam and the Republic of the Philippines).

In connection with the Pfizer Purchase Agreement, Pfizer purchased 2,362,348 shares of the Company's common stock at a price of $16.93 per share for a total investment of $40.0 million. The Company received no other upfront payments but is eligible to receive up to $80.0 million in development and sales milestones, and may also receive high single-digit to low double-digit royalties on net sales of SPR206 in the Pfizer Territory. Achievement of these payments cannot be guaranteed. The Company and Pfizer agree that upon Pfizer's request, the parties will negotiate in good faith regarding procuring a clinical or commercial supply of the compound.

Under the Pfizer Purchase Agreement, the fair market value of the 2,362,348 shares of the Company's common stock issued to Pfizer was determined to be $27.5 million, which was valued using an option pricing valuation model as the shares are subject to certain holding period restrictions. The Company accounted for the associated premium of $12.5 million as a freestanding equity-linked instrument under ASC 815. The premium was allocated as consideration for the Pfizer License Agreement and evaluated under ASC 606. The premium was determined not to be constrained and was included in the calculation of the total transaction price related to the Pfizer License Agreement as of June 30, 2021.

The Company is responsible for all costs related to developing and obtaining regulatory approval of SPR206 and Pfizer Licensed Products in the Pfizer Territory, with a focus on the European market, and is obligated to use commercially reasonable efforts, including to achieve certain specified diligence milestones within agreed-upon periods. A joint development committee was established between the Company and Pfizer to coordinate and review the development, manufacturing and commercialization plans with respect to Pfizer Licensed Products in the Pfizer Territory. Pfizer is responsible for commercializing SPR206 and the Pfizer Licensed Products in the Pfizer Territory.

Unless earlier terminated due to certain material breaches of the contract or by Pfizer's convenience, or otherwise, the Pfizer License Agreement will expire on a jurisdiction-by-jurisdiction and licensed product-by-licensed product basis after ten years from the effective date. The Pfizer License Agreement will automatically renew for an additional ten-year term unless terminated.

Accounting Analysis and Revenue Recognition

The Company determined that Pfizer is a customer and that the Pfizer License Agreement is within the scope of ASC 606 as licensing intellectual property and performing ongoing research and development services are ordinary activities that are ongoing and central to the Company's operations. 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 two performance obligations, license and know-how transfer and research and development services related to upcoming milestones. The Company determined that the supply agreement is a customer option and not a material right, as the pricing to Pfizer is not at a significant discount. Furthermore, Pfizer has the right to use third parties to manufacture the compound, or to manufacture the compound itself.

At contract inception, $1.4 million of the then transaction price of $12.5 million was allocated to the license and know-how transfer performance obligations, which was fully satisfied and recognized as revenue upon delivery of the license. The additional $11.1 million was allocated to the research and development services obligation and is being recognized over time as services are delivered.

In the third quarter of 2022, upon the completion of a milestone related to regulatory engagement for SPR206, Pfizer communicated its approval that the milestone was achieved, and the Company received $5.0 million under the Pfizer License Agreement, which the Company accounted for as variable consideration under ASC 606 and was added to the transaction price in the third quarter of 2022. Of this $5.0 million milestone, $0.9 million was recognized during the third quarter of 2022 and the remaining $4.1 million was allocated to the research and development services performance obligation and is recognized over time as the services are delivered.

The potential license maintenance fees and development milestone payments from the Pfizer License Agreement will be accounted for as variable consideration under ASC 606. Given the uncertain nature of these payments, the Company determined they were fully constrained as of December 31, 2024 and not included in the transaction price. The Company can also earn sales-based royalties.

The Company recognizes revenue for the license performance obligation at a point in time, that is upon transfer of the license to Pfizer. Control of the license was transferred on the Effective Date and Pfizer could begin to use and benefit from the license at the Effective Date.

In total, and inclusive of the above, the Company recognized $0.4 million and $0.9 million of revenue from the contract during the years ended December 31, 2024 and 2023, respectively.

The remaining transaction price balance of approximately $12.6 million from the Pfizer Purchase Agreement allocated to the research and development services performance obligation has been recorded as deferred revenue in the consolidated balance sheets. As of December 31, 2024, the research and development services related to the second performance obligation are expected to be recognized as costs are incurred over the project development timeframe.

14. Segment Information

The Company manages its operations as a single operating segment for the purpose of assessing performance and making operating decisions, resulting in a single reportable segment. The Company's singular focus is on identifying and developing novel treatments for bacterial infections, including MDR bacterial infections, and rare diseases. The Company earns revenue from collaboration agreements with third parties and grant revenue in connection with various government awards. The Company has determined that its Chief Operating Decision Maker ("CODM") is its Chief Executive Officer. The CODM reviews the Company's financial information on a consolidated basis for the purpose of allocating resources and assessing financial performance. The measure of segment assets is reported on the balance sheet as total consolidated assets. All of the Company's tangible assets are held in the United States.

The accounting policies for the operating segment are consistent with the Company's policies for the Consolidated Financial Statements. The key measure of segment profit or loss that the CODM uses to allocate resources and assess performance is the Company's consolidated profit or loss, as reported on the consolidated statements of operations and comprehensive loss. This is reviewed against budgeted expectations to assess segment performance and allocate resources. The Company's reportable segment net revenues, significant segment expenses and consolidated profit (loss) for the years ended December 31, 2024 and 2023, consisted of the following:

	Year Ended December 31,	
	2024	2023
Revenues:		
Grant Revenue	$ 20,581	$ 7,046
Collaboration revenue - related party	27,025	95,802
Collaboration revenue	371	933
Total revenues	47,977	103,781
Less:		
Tebipenem HBr	60,502	16,695
SPR720	16,626	13,031
SPR206	570	3,240
Research and development personnel related (including share-based compensation)	14,111	13,788
Facility related and other, research and development	4,948	4,686
General and administrative personnel related (including share-based compensation)	13,188	15,324
Professional and consultant fees	8,198	8,151
Facility related and other, general and administrative	2,318	2,079
Other segment items*	817	5,320
Interest income	(4,735)	(3,937)
Income tax expense	-	2,598
Consolidated profit (loss)	$ (68,566)	$ 22,806

*Other segment items include restructuring charges (see Note 9), impairment of long-term asset and other income, net.

15. Net Income (Loss) per Share

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

	Year Ended December 31,	
	2024	2023
Numerator:		
Net income (loss)	$ (68,566)	$ 22,806
Denominator:		
Basic weighted average common shares outstanding	54,037,917	52,703,467
Effect of dilutive securities	—	285,563
Diluted weighted-average common shares outstanding	54,037,917	52,989,030
Net income (loss) per share, basic	$ (1.27)	$ 0.43
Net income (loss) per share, diluted	$ (1.27)	$ 0.43

The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net income (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,	
	2024	2023
Options to purchase common stock	2,814,850	3,485,373
Unvested RSUs and PSUs	6,038,732	3,462,595
Total	8,853,582	6,947,968

16. Retirement Plan

The Company has a defined-contribution plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pre-tax basis. As currently established, the Company is not required to make any contributions to the 401(k) Plan. The Company made matching contributions to the 401(k) Plan of $0.3 million during both the years ended December 31, 2024 and 2023, respectively.

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 Interim Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer) evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2024. 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 (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, 2024, our Interim 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 *Internal Control – Integrated Framework* (2013) 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, 2024.

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, 2024 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Trading Arrangements

None of our directors or officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement (as defined in Item 408(c) of Regulation S-K) during fiscal year 2024.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

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” and “Code of Conduct and Ethics” in the Company’s proxy statement for the 2025 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 2025 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 2025 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 2025 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 Accountant 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 2025 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	Certificate of Amendment to the Amended and Restated Certificate of Incorporation of the Registrant		Form 8-K (Exhibit 3.1)	8/18/2021	001-38266
3.3	Amended and Restated Bylaws of the Registrant		Form 10-Q (Exhibit 3.1)	11/13/2023	001-38266
3.4	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
3.5	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
3.6	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
3.7	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	Description of Registrant's Securities		Form 10-K (Exhibit 4.2)	3/30/2023	001-38266
10.1#	2017 Stock Incentive Plan, as amended		Form 8-K (Exhibit 10.1)	6/3/2024	001-38266
10.2#	Form of Stock Option Agreement under the 2017 Stock Incentive Plan, as amended		Form S-8 (Exhibit 4.6)	9/20/2021	333-259662
10.3#	Form of Restricted Stock Unit Agreement under the 2017 Stock Incentive Plan, as amended		Form 8-K (Exhibit 10.1)	8/30/2021	001-38266
10.4#	2019 Inducement Equity Incentive Plan, as amended		Form 10-K (Exhibit 10.4)	3/13/2024	001-38266
10.5#	Form of Stock Option Agreement under the 2019 Inducement Equity Incentive Plan, as amended		Form S-8 (Exhibit 4.6)	8/10/2023	333-273880
10.6#	Form of Restricted Stock Unit Agreement under the 2019 Inducement Equity Incentive Plan, as amended		Form S-8 (Exhibit 4.7)	8/10/2023	333-273880

10.7#	Form of Director and Officer Indemnification Agreement		Form S-1 (Exhibit 10.4)	10/6/2017	333-220858
10.8#	Non-Employee Director Compensation Policy, as amended		Form 10-K (Exhibit 10.8)	3/13/2024	001-38266
10.9#	Consulting Agreement, dated June 13, 2023, by and between the Registrant and Ankit Mahadevia, M.D.		Form 10-Q (Exhibit 10.2)	8/10/2023	001-38266
10.10#	Amendment and Restated Employment Agreement, dated June 13, 2023, by and between the Registrant and Satyavrat Shukla		Form 10-Q (Exhibit 10.3)	8/10/2023	001-38266
10.11#	Interim Period Agreement, dated January 10, 2025, by and between the Registrant and Satyavrat Shukla		Form 8-K (Exhibit 10.1)	1/10/2025	001-38266
10.12#	Retention Letter Agreement, dated November 13, 2024, by and between the Registrant and Satyavrat Shukla	X			
10.13#	Employment Agreement, dated August 11, 2022, by and between the Registrant and Kamal Hamed, M.D.		Form 10-Q (Exhibit 10.5)	11/14/2022	001-38266
10.14#	Amendment to Employment Agreement, dated November 10, 2022, by and between the Registrant and Kamal Hamed, M.D.		Form 10-Q (Exhibit 10.8)	11/14/2024	001-38266
10.15#	Separation Agreement, dated July 30,2024 by and between the Registrant and Kamal Hamed, M.D.		Form 10-Q (Exhibit 10.1)	11/14/2024	001-38266
10.16#	Separation Agreement, dated July 30,2024 by and between the Registrant and Kamal Hamed, M.D.		Form 10-K (Exhibit 10.12)	3/16/2020	001-38266
10.17#	Amendment to Employment Agreement, dated November 10, 2022, by and between the Registrant and Timothy Keutzer		Form 10-Q (Exhibit 10.9)	11/14/2022	001-38266
10.18#	Second Amendment to Employment Agreement, dated as of February 1, 2023, by and between the Registrant and Timothy Keutzer		Form 10-Q (Exhibit 10.1)	5/11/2023	001-38266
10.19#	Retention Letter Agreement, dated November 13, 2024, by and between the Registrant and Timothy Keutzer	X			
10.20#	Employment Agreement, dated October 31, 2023 by and between the Registrant and Esther Rajavelu		Form 10-Q (Exhibit 10.1)	5/11/2024	001-38266
10.21#	Interim Period Agreement, dated January 10, 2025, by and between the Registrant and Esther Rajavelu		Form 8-K (Exhibit 10.2)	1/10/2025	001-38266
10.22#	Retention Letter Agreement, dated November 13, 2024, by and between the Registrant and Esther Rajavelu	X			
10.23#	Employment Agreement, dated November 6, 2020, by and between the Registrant and Tamara Joseph		Form 10-K (Exhibit 10.13)	3/11/2021	001-38266
10.24#	Amendment to Employment Agreement, dated November 10, 2022, by and between the Registrant and Tamara Joseph		Form 10-Q (Exhibit 10.10)	11/14/2022	001-38266
10.25#	Separation Agreement, dated February 9, 2024, by and between the Registrant and Tamara Joseph		Form 10-K (Exhibit 10.34)	3/13/2024	001-38266

10.26#	Consulting Agreement, dated February 9, 2024, by and between the Registrant and Tamara Joseph		Form 10-K (Exhibit 10.34)	3/13/2024	001-38266
10.27#	Consulting Agreement, effective as of August 5, 2024, by and between the Registrant and John C. Pottage, Jr., M.D.		Form 10-Q (Exhibit 10.3)	11/14/2024	001-38266
10.28#	Amended and Restated Consulting Agreement, effective as of January 29, 2025, by and between the Registrant and John C. Pottage, Jr., M.D.	X			
10.29#	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
10.30	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
10.31	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
10.32	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
10.33	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
10.34†	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
10.35†	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
10.36†	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
10.37†	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
10.38††	Amended and Restated License Agreement, dated January 15, 2021, by and between the Registrant and Everest Medicines II Limited		Form 10-K (Exhibit 10.25)	3/11/2021	001-38266
10.39††	License Agreement, dated June 30, 2021, by and between the Registrant and Pfizer Inc.		Form 10-Q (Exhibit 10.1)	8/5/2021	001-38266
10.40	Share Purchase Agreement, dated June 30, 2021, by and between the Registrant and Pfizer Inc.		Form 10-Q (Exhibit 10.2)	8/5/2021	001-38266
10.41††	Exclusive License Agreement, dated September 21, 2022, by and between the Registrant and GlaxoSmithKline Intellectual Property (No. 3) Limited		Form 10-Q (Exhibit 10.3)	11/14/2022	001-38266

10.42††	Amendment 1 to Exclusive License Agreement, dated July 4, 2023, by and between the Registrant and GlaxoSmithKline Intellectual Property (No. 3) Limited		Form 10-K (Exhibit 10.34)	3/13/2024	001-38266
10.43††	Amendment 2 to Exclusive License Agreement, dated December 20, 2023, by and between the Registrant and GlaxoSmithKline Intellectual Property (No. 3) Limited		Form 10-K (Exhibit 10.34)	3/13/2024	001-38266
10.44††	Amendment 3 to Exclusive License Agreement, dated March 4, 2024, by and between the Registrant and GlaxoSmithKline Intellectual Property (No. 3) Limited		Form 10-Q (Exhibit 10.4)	5/15/2024	001-38266
10.45††	Amendment 4 to Exclusive License Agreement, dated October 28, 2024, by and between the Registrant and GlaxoSmithKline Intellectual Property (No. 3) Limited		Form 10-Q (Exhibit 10.3)	11/14/2024	001-38266
10.47	Share Purchase Agreement, dated September 21, 2022, by and between the Registrant and Glaxo Group Limited		Form 10-Q (Exhibit 10.4)	11/14/2022	001-38266
10.48	Controlled Equity Offering Sales Agreement, dated March 11, 2021, by and between the Registrant and Cantor Fitzgerald & Co.		Form 10-K (Exhibit 10.28)	3/11/2021	001-38266
10.49	Form of Proprietary Information and Inventions Assignment Agreement		Form S-1/A (Exhibit 10.17)	10/23/2017	333-220858
19.1	Spero Therapeutics, Inc. Insider Trading Policy, effective as of June 5, 2023	X			
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			
97.1	Clawback Policy, effective as of November 12, 2023		Form 10-K (Exhibit 97.1)	3/13/2024	001-38266
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) is the type that the Registrant treats as private or confidential.

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 27, 2025

By: /s/ Esther Rajavelu
Esther Rajavelu
Interim Chief Executive Office

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Esther Rajavelu or her true and lawful attorney-in-fact and agent, with full power of substitution, for her and in her 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 she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or her substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

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/ Esther Rajavelu Esther Rajavelu	Interim Chief Executive Officer, Chief Financial Officer, Chief Business Officer and Treasurer *(Principal Executive, Financial and Accounting Officer)*	March 27, 2025
/s/ Milind Deshpande, Ph.D. Milind Deshpande, Ph.D.	Director	March 27, 2025
/s/ Scott Jackson Scott Jackson	Director	March 27, 2025
/s/ John C. Pottage, M.D. John C. Pottage, M.D.	Director	March 27, 2025
/s/ Cynthia Smith Cynthia Smith	Director	March 27, 2025
/s/ Frank E. Thomas Frank E. Thomas	Director	March 27, 2025
/s/ Kathleen Tregoning Kathleen Tregoning	Director	March 27, 2025
/s/ Patrick Vink, M.D. Patrick Vink, M.D.	Director	March 27, 2025

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Directors

Frank E. Thomas
Chairman of the Board of Directors, Spero Therapeutics, Inc.
President and Chief Operating Officer, Orchard Therapeutics plc

Ankit Mahadevia, M.D.
Chief Experience Officer, Curie.Bio Operations, LLC

Cynthia Smith
Director, Agios Pharmaceuticals, Inc., Protara Therapeutics, Inc., and Akebia Therapeutics, Inc.

Satyavrat Shukla
President and Chief Executive Officer of Spero Therapeutics, Inc. (serving until May 2, 2025)

Patrick Vink, M.D.
Senior Advisor, Athyrium Capital Management, LP

Milind Deshpande, Ph.D.
Venture Partner, RA Capital Management, LLC

Scott Jackson
Chairman of the Board of Directors, Mural Oncology plc
Director, GlycoMimetics, Inc. and MacroGenics, Inc.

John C. Pottage, Jr., M.D.
Lead Scientific Consultant, Intrepid Alliance Inc.

Kathleen Tregoning
Former Chief Corporate Affairs Officer of Cerevel Therapeutics Holdings, Inc.

Executive Officers

Esther Rajavelu
Interim President and Chief Executive Officer, Chief Financial Officer, Chief Business Officer and Treasurer (full-time President and Chief Executive Officer as of May 2, 2025)

Timothy Keutzer
Chief Operating Officer

Stockholders and Stock Listing

Our common stock is traded on The Nasdaq Global Select Market under the symbol SPRO.

Investor Information

You may obtain a copy of any of the exhibits to our Annual Report on Form 10-K free of charge. These documents are available on our website at www.sperotherapeutics.com or by contacting Investor Relations at Spero Therapeutics, Inc.

Requests for information about Spero Therapeutics, Inc. should be directed to:

Investor Relations
Spero Therapeutics, Inc.
675 Massachusetts Avenue, 14th Floor
Cambridge, MA 02139
Telephone: (857) 242-1600

Annual Meeting

The 2025 annual meeting of stockholders will be held virtually via live webcast on Thursday, June 12, 2025 at 9:00 a.m. ET.

You will be able to attend our annual meeting, vote and submit your questions during the meeting by visiting www.virtualshareholdermeeting.com/SPRO2025.

Internet Website

www.sperotherapeutics.com

Legal Counsel

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

Independent Registered Public Accounting Firm

PricewaterhouseCoopers LLP

Transfer Agent and Registrar

Computershare Trust Company, N.A.
150 Royall Street
Canton, MA 02021

Spero Therapeutics, Inc.
675 Massachusetts Avenue, 14th Floor
Cambridge, MA 02139
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