UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended March 31, 2019

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

Commission File Number 001-38266

SPERO THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

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

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

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

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

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

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

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

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

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

As of May 6, 2019, the registrant had 17,523,835 shares of common stock, $0.001 par value per share, outstanding.

FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q 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 Quarterly Report on Form 10-Q are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

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

Any forward-looking statements in this Quarterly Report on Form 10-Q reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Part II, Item 1A. "Risk Factors" and elsewhere in this Quarterly Report on Form 10-Q. 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 Quarterly Report on Form 10-Q 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.

Spero Therapeutics, Inc.
Table of Contents

		Page
	PART I – FINANCIAL INFORMATION	
Item 1.	Financial Statements (Unaudited)	3
	Condensed Consolidated Balance Sheets as of March 31, 2019 and December 31, 2018	3
	Condensed Consolidated Statements of Operations and Comprehensive Loss for the three months ended March 31, 2019 and 2018	4
	Condensed Consolidated Statements of Cash Flows for the three months ended March 31, 2019 and 2018	5
	Condensed Consolidated Statements of Stockholders' Equity for the three months ended March 31, 2019 and 2018	6
	Notes to Unaudited Condensed Consolidated Financial Statements	7
Item 2.	Management's Discussion and Analysis of Financial Condition and Results of Operations	23
Item 3.	Quantitative and Qualitative Disclosures About Market Risk	35
Item 4.	Controls and Procedures	35
	PART II – OTHER INFORMATION	
Item 1A.	Risk Factors	36
Item 2.	Unregistered Sales of Equity Securities and Use of Proceeds	71
Item 6.	Exhibits	71
	Signatures	72

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

SPERO THERAPEUTICS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share data)
(Unaudited)

	March 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 49,395	$ 34,080
Marketable securities	56,997	81,363
Other receivables	456	376
Tax incentive receivable, current	928	922
Prepaid expenses and other current assets	7,926	7,478
Total current assets	115,702	124,219
Property and equipment, net	2,864	2,893
Tax incentive receivable	294	233
Operating lease right of use assets	4,369	—
Other assets	1,421	1,661
Total assets	$ 124,650	$ 129,006
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 557	$ 3,603
Accrued expenses and other current liabilities	5,199	8,263
Derivative liabilities	223	223
Deferred rent	—	229
Current operating lease liabilities	639	—
Total current liabilities	6,618	12,318
Deferred rent, net of current portion	—	833
Non-current operating lease liabilities	4,391	—
Other long-term liabilities	312	—
Total liabilities	11,321	13,151
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized, 3,220 shares issued and outstanding as of March 31, 2019 and December 31, 2018	—	—
Common stock, $0.001 par value; 60,000,000 shares authorized as of March 31, 2019 and December 31, 2018;17,335,066 shares issued and outstanding as of March 31, 2019 and 17,205,962 shares issued and outstanding as of December 31, 2018	17	17
Additional paid-in capital	256,530	254,013
Accumulated deficit	(143,574)	(138,502)
Accumulated other comprehensive gain (loss)	1	(28)
Total Spero Therapeutics, Inc. stockholders' equity	112,974	115,500
Non-controlling interests	355	355
Total stockholders' equity	113,329	115,855
Total liabilities and stockholders' equity	$ 124,650	$ 129,006

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

SPERO THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share data)
(Unaudited)

	Three Months Ended March 31,	
	2019	2018
Revenues:		
Grant revenue	$ 3,911	$ 1,153
Collaboration revenue	3,807	—
Total revenues	7,718	1,153
Operating expenses:		
Research and development	9,526	8,925
General and administrative	3,888	3,044
Total operating expenses	13,414	11,969
Loss from operations	(5,696)	(10,816)
Other income (expense):		
Interest income and other income (expense), net	624	172
Total other income (expense), net	624	172
Net loss	$ (5,072)	$ (10,644)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.29)	$ (0.74)
Weighted average common shares outstanding, basic and diluted:	17,221,120	14,369,182
Comprehensive loss:		
Net loss	(5,072)	(10,644)
Other comprehensive gain (loss):		
Unrealized gain (loss) on marketable securities	23	(29)
Reclassification adjustment for gains included in net loss	6	—
Net unrealized gains (losses) on securities	29	(29)
Total comprehensive loss	$ (5,043)	$ (10,673)

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

SPERO THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)
(Unaudited)

	Three Months Ended March 31,	
	2019	2018
Cash flows from operating activities:		
Net loss	$ (5,072)	$ (10,644)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	184	95
Share-based compensation	933	614
Realized (gain) loss on investments	(1)	—
Unrealized foreign currency transaction (gain) loss	(95)	8
Accretion of discount on marketable securities	(355)	(45)
Changes in operating assets and liabilities:		
Other receivables	(80)	(208)
Prepaid expenses and other current assets	(448)	604
Tax incentive receivables	(62)	(45)
Other assets	433	—
Accounts payable	(3,008)	(2,469)
Accrued expenses and other current liabilities	(3,364)	165
Deferred rent	—	(36)
Other long-term liabilities	11	—
Net cash used in operating activities	(10,924)	(11,961)
Cash flows from investing activities:		
Purchases of marketable securities	(25,835)	(22,825)
Proceeds from maturities of marketable securities	50,587	—
Purchases of property and equipment	(81)	—
Net cash provided by (used in) investing activities	24,671	(22,825)
Cash flows from financing activities:		
Proceeds from the issuance of common stock, net of issuance costs	1,525	—
Payment of offering costs	(16)	—
Proceeds from stock option exercises	59	—
Net cash provided by financing activities	1,568	—
Net increase (decrease) in cash and cash equivalents	15,315	(34,786)
Cash, cash equivalents and restricted cash at beginning of period	34,080	87,338
Cash, cash equivalents and restricted cash at end of period	$ 49,395	$ 52,552
Supplemental disclosure of non-cash investing and financing activities:		
Purchases of property and equipment included in accounts payable and accrued expenses	$ 75	$ —

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

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

	Series A and B Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Accumulated Other Comprehensive	Spero Therapeutics, Inc. Stockholders'	Non-controlling	Total Stockholders'
	Shares	Par Value	Shares	Par Value	Capital	Deficit	(Loss)	Equity	Interests	Equity
Balances at December 31, 2018	**3,220**	**$ —**	**17,205,962**	**$ 17**	**$ 254,013**	**$ (138,502)**	**$ (28)**	**$ 115,500**	**$ 355**	**$ 115,855**
Issuance of common stock upon the exercise of stock options	—	—	10,014	—	59	—	—	59	—	59
Issuance of common stock, net of issuance costs	—	—	119,090	—	1,525	—	—	1,525	—	1,525
Share-based compensation expense	—	—	—	—	933	—	—	933	—	933
Unrealized gain (loss) on available-for-sale securities	—	—	—	—	—	—	29	29	—	29
Net loss	—	—	—	—	—	(5,072)	—	(5,072)	—	(5,072)
Balances at March 31, 2019	**3,220**	**$ —**	**17,335,066**	**$ 17**	**$ 256,530**	**$ (143,574)**	**$ 1**	**$ 112,974**	**$ 355**	**$ 113,329**

	Series A and B Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Accumulated Other Comprehensive	Spero Therapeutics, Inc. Stockholders'	Non-controlling	Total Stockholders'
	Shares	Par Value	Shares	Par Value	Capital	Deficit	(Loss)	Equity	Interests	Equity
Balances at December 31, 2017	**—**	**$ —**	**14,369,182**	**$ 14**	**$ 181,428**	**$ (96,840)**	**$ —**	**$ 84,602**	**$ 355**	**$ 84,957**
Share-based compensation expense	—	—	—	—	614	—	—	614	—	614
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	(29)	(29)	—	(29)
Net loss	—	—	—	—	—	(10,644)	—	(10,644)	—	(10,644)
Balances at March 31, 2018	**—**	**$ —**	**14,369,182**	**$ 14**	**$ 182,042**	**$ (107,484)**	**$ (29)**	**$ 74,543**	**$ 355**	**$ 74,898**

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

SPERO THERAPEUTICS, INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
(Unaudited)

1. Nature of the Business and Basis of Presentation

Spero Therapeutics, Inc., together with its consolidated subsidiaries (the "Company" or "Spero"), is a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing and commercializing novel treatments for multi-drug resistant ("MDR") bacterial infections. The Company's most advanced product candidate, SPR994, is designed to be the first broad-spectrum oral carbapenem-class antibiotic for use in adults to treat MDR Gram-negative infections. Treatment with effective orally administrable antibiotics may prevent hospitalizations for serious infections and enable earlier, more convenient and cost-effective treatment of patients after hospitalization. The Company is also developing SPR720, an oral antibiotic designed for the treatment of pulmonary non-tuberculous mycobacterial ("NTM") infections. In addition, the Company also has a platform technology known as its Potentiator Platform that it believes will enable it to develop drugs that will expand the spectrum and potency of existing antibiotics, including formerly inactive antibiotics, against Gram-negative bacteria. The Company's product candidates generated from its Potentiator Platform are two intravenous, or IV,-administered agents, SPR206 and SPR741, designed to treat MDR Gram-negative infections in the hospital setting. The Company believes that its novel product candidates, if successfully developed and approved, would have a meaningful patient impact and significant commercial applications for the treatment of MDR infections in both the community and hospital settings.

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

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

In accordance with Accounting Standards Update ("ASU") 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued. Since inception, the Company has funded its operations with proceeds from sales of preferred units (including bridge units, which converted into preferred units), payments received in connection with a concluded collaboration agreement, funding from government contracts, a licensing agreement and through the sale of our common and preferred stock. The Company has incurred recurring losses since inception. As of March 31, 2019, the Company had an accumulated deficit of $143.6 million. The Company expects to continue to generate operating losses for the foreseeable future. As of the issuance date of the quarterly consolidated financial statements, or May 9, 2019, the Company expects that its cash, cash equivalents and marketable securities will be sufficient to fund its operating expenses, capital expenditure requirements through at least 12 months from the issuance date of these quarterly consolidated financial statements. However, the future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its future operations. The Company will seek additional funding through public or private financings, debt financing, collaboration agreements or government grants. The inability to obtain funding, as and when needed, would have a negative impact on the Company's financial condition and ability to pursue its business strategies. If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects, or the Company may be unable to continue operations. Although management intends to pursue plans to obtain additional funding to finance its operations, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

The accompanying consolidated financial statements 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.

Interim Financial Information

The consolidated balance sheet at December 31, 2018 was derived from audited financial statements, but does not include all disclosures required by GAAP. The accompanying unaudited condensed consolidated financial statements as of March 31, 2019, and for the three months ended March 31, 2019 and 2018, have been prepared by the Company pursuant to the rules and regulations of the Securities and Exchange Commission ("SEC") for interim financial statements. Certain information and footnote disclosures normally included in financial statements prepared in accordance with GAAP have been condensed or omitted pursuant to such rules and regulations. These consolidated financial statements should be read in conjunction with the Company's audited consolidated financial statements and the notes thereto for the year ended December 31, 2018, included in the Company's Annual Report on Form 10-K for the year ended December 31, 2018, on file with SEC. In the opinion of management, all adjustments, consisting only of normal recurring adjustments necessary for a fair statement of the Company's financial position as of March 31, 2019, and results of operations for the three months ended March 31, 2019 and 2018, and cash flows for the three months ended March 31, 2019 and 2018 have been made. The results of operations for the three months ended March 31, 2019 are not necessarily indicative of the results of operations that may be expected for the year ending December 31, 2019.

2. Summary of Significant Accounting Policies

Use of Estimates

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

Cash Equivalents

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

Marketable Securities

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

Fair Value Measurements

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

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

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

Revenue Recognition – Collaboration Revenue

Effective January 1, 2019, the Company entered into a licensing agreement that is 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. Any future out-licensing agreements entered into by the Company and additional third parties shall also be evaluated under Topic 606. 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. The Company assessed its revenue-generating arrangement in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in the arrangement. 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. These assumptions may include forecasted revenues, development timelines, discount rates and probabilities of technical and regulatory success.

Leases

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

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

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

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

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

after, the Company has elected to account for the lease and non-lease components for leases for classes of all underlying assets and allocate all of the contract consideration to the lease component only.

Net Income (Loss) per Share

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

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

Recently Issued and Adopted Accounting Pronouncements

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

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

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

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

within those fiscal years. The Company adopted the ASU effective January 1, 2019. The adoption of ASU 2017-11 did not have a material impact on the Company's consolidated financial statements.

In June 2018, the FASB issued ASU 2018-07, *Compensation—Stock Compensation (Topic 718) – Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"), which aligns the accounting for share-based payment awards issued to employees and nonemployees. Under the new guidance, the existing employee guidance will apply to nonemployee share-based transactions (as long as the transaction is not effectively a form of financing), with the exception of specific guidance related to the attribution of compensation cost. The cost of nonemployee awards will continue to be recorded as if the grantor had paid cash for the goods or services. In addition, the contractual term will be able to be used in lieu of an expected term in the option-pricing model for nonemployee awards. The amendments in the new guidance are effective for public entities for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. Early adoption is permitted, including in interim periods, but no earlier than an entity's adoption of ASC 606. The Company adopted the ASU effective January 1, 2019. The adoption of ASU 2018-07 did not have a material impact on the Company's consolidated financial statements.

3. Fair Value Measurements and Marketable Securities

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

	Fair Value Measurements at March 31, 2019 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ —	$ 38,575	$ —	$ 38,575
Commercial paper	—	6,684	—	6,684
Total cash equivalents	—	45,259	—	45,259
Marketable securities:				
U.S. government securities	—	25,382	—	25,382
Corporate bonds	—	9,141	—	9,141
Commercial paper	—	22,474	—	22,474
Total marketable securities	—	56,997	—	56,997
Total cash equivalents and marketable securities	$ —	$ 102,256	$ —	$ 102,256
Liabilities:				
Derivative liabilities:				
Anti-dilution rights	$ —	$ —	$ 223	$ 223
	$ —	$ —	$ 223	$ 223

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

Excluded from the tables above is cash of $4.1 million and $5.4 million as of as of March 31, 2019, and December 31, 2018, respectively. During the three months ended March 31, 2019, there were no transfers between Level 1, Level 2 and Level 3 categories.

Marketable Securities

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

The following table summarizes the gross unrealized gains and losses of the Company's marketable securities as of March 31, 2019, and December 31, 2018 (in thousands):

	March 31, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets:				
U.S. government securities	$ 25,381	$ 2	$ (1)	$ 25,382
Corporate bonds	9,141	—	—	9,141
Commercial paper	22,474	—	—	22,474
	$ 56,996	$ 2	$ (1)	$ 56,997

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

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

Anti-Dilution Rights

In connection with the issuance of non-controlling interests in certain of the Company's subsidiaries (see Note 8), specifically Spero Potentiator, Inc., Spero Europe, Ltd. and Spero Gyrase, Inc., the Company granted anti-dilution rights to the minority investors. The Company classifies the anti-dilution rights as a derivative liability on its consolidated balance sheet because they are freestanding instruments that represent a conditional obligation to issue a variable number of shares. The Company remeasures the derivative liability associated with the anti-dilution rights to fair value at each reporting date, and recognizes changes in the fair value of the derivative liability as a component of other income (expense) in the consolidated statement of operations and comprehensive loss. The fair value of these derivative liabilities was determined using a discounted cash flow model. As of March 31, 2019 and December 31, 2018, the Company's fair value of the anti-dilution rights of $0.2 million relates only to the anti-dilution rights held by the minority investor in Spero Gyrase, Inc., which represents amounts funded to the entity that could be settled by the issuance of equity.

Spero Gyrase, Inc.

In March 2016, in connection with the issuance of a non-controlling interest in its subsidiary, Spero Gyrase, Inc. ("Spero Gyrase"), to Biota Pharmaceuticals, Inc. (now Aviragen Therapeutics, Inc.) ("Aviragen"), the Company granted to Aviragen certain anti-dilution rights (see Note 8). The fair value of the derivative liability related to the anti-dilution rights upon issuance in March 2016 was $1.6 million.

The most significant assumption impacting the fair value of the anti-dilution rights was the probability that the Company would fund the maximum amount of investment providing anti-dilution protection. Upon issuance of the rights and through December 31, 2016, the probability of such funding was determined to be 100%. During 2017, the probability of such funding was reduced to 0%

due to the Company's decision to no longer pursue development of the acquired technology. The fair value of the derivative liability decreased accordingly by $1.4 million to $0.2 million by June 30, 2017. As of March 31, 2019 and December 31, 2018, the value of the derivative liability of $0.2 million represents amounts funded to the entity that could be settled by the issuance of equity.

4. Leases

Operating Leases

In August 2015, the Company entered into an operating lease agreement with U.S. REIF Central Plaza Massachusetts, LLC (the "Landlord") with respect to its corporate headquarters located at 675 Massachusetts Avenue, Cambridge, Massachusetts (the "Original Lease").The term of the Original Lease commenced in January 2016 and was scheduled to expire in December 2020. The Original Lease required annual payments of $0.4 million, subject to certain escalations described below, over the initial five-year term, with a renewal option to extend its term for an additional five years. Under the terms of the Original Lease, the Company provided a security deposit of $0.2 million to the Landlord, which is included in long-term assets in the accompanying condensed consolidated balance sheets. The Original Lease provided for annual rent escalations as well as tenant incentives in the amount of $0.7 million, of which $0.3 million would be reimbursed to the Landlord over the initial term of the Original Lease. In determining its ROU assets as of January 1, 2019, the Company reduced the amount of ROU assets by $0.2 million, which was the remaining balance of lease incentives received from the Landlord as of that date. The lease does not include any restrictions or covenants that had to be accounted for under the lease guidance.

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

On January 17, 2018, the Company entered into an amendment to the Original Lease (the "Amendment"). The Amendment makes certain modifications to the Original Lease, including (i) the addition of approximately 7,800 square feet of office space in the same building (the "Expansion Premises") and (ii) an extension of the expiration date of the Original Lease to seven years following the delivery date of the Expansion Premises (the "Lease Term"), which occurred on December 22, 2018.

Under the Amendment, the Company has two consecutive options to extend the Lease Term for an additional period of five years (the "Option Terms"), subject to certain conditions, upon notice to the Landlord. The Amendment provides for annual base rent for the Expansion Premises of approximately $0.5 million in the first year of the Lease Term, which increases on an annual basis to approximately $0.6 million in the final year of the Lease Term, and annual base rent during the Option Terms to be calculated based on the Landlord's good faith determination of 100% of the fair market rate for such Option Terms. The Company is also obligated to pay the Landlord certain costs, taxes and operating expenses, subject to certain exclusions. The Amendment also provides for $0.4 million from the Landlord for leasehold improvements on the Expansion Premises. In determining its ROU assets as of January 1, 2019, the Company reduced the amount of ROU assets by $0.4 million, which was the remaining balance of lease incentives received from the Landlord as of that date. The lease does not include any restrictions or covenants that had to be accounted for under the lease guidance.

For the three months ended March 31, 2019, the components of operating lease expense were as follows (in thousands):

Operating lease expense	Statement of Operations Location	Amount
Fixed operating lease expense	Research and development expense	145
	General and administrative expense	171
Variable operating lease expense	Research and development expense	13
	General and administrative expense	48
Total operating lease expense		$ 377

Supplemental cash flow information related to the Company's operating leases for the three-month period ended March 31, 2019 was as follows (in thousands):

	March 31, 2019
Cash paid for amounts included in the measurement of lease liabilities:	
Operating cash flows from operating leases	$ 316

Embedded Finance Leases

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

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

Lease Assets and Liabilities	Classification	March 31, 2019
Assets		
Operating	Operating lease right of use assets	$ 4,369
Financing	Property and equipment, net	1,426
Total leased assets		$ 5,795
Liabilities		
Current		
Operating	Current operating lease liabilities	$ 639
Non-Current		
Operating	Non-current operating lease liabilities	4,391
Total lease liabilities		$ 5,030
Weighted average remaining lease term		6 years
Weighted average discount rate		11%

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

Years Ending December 31,	
2019 (remainder)	$ 918
2020	928
2021	943
2022	1,061
2023	1,076
2024	1,092
Thereafter	1,108
Total future minimum lease payments	7,126
Less imputed interest	(2,096)
Total operating lease liabilities	$ 5,030

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

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

5. Accrued Expenses and Other Current Liabilities

	March 31, 2019	December 31, 2018
Accrued external research and development expenses	$ 3,209	$ 4,541
Accrued payroll and related expenses	885	2,379
Accrued professional fees	470	917
Accrued other	635	426
	$ 5,199	$ 8,263

6. Common Stock

On December 3, 2018, the Company filed a universal shelf registration statement on Form S-3 (Registration No. 333-228661) with the SEC, which was declared effective on December 11, 2018, pursuant to which it registered for sale up to $200.0 million of any combination of its common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that the Company may determine, including up to $50.0 million of its common stock available for issuance pursuant to an at-the-market offering program sales agreement that it entered into with Cantor Fitzgerald & Co. ("Cantor"). Under the sales agreement, Cantor may sell shares of the Company's common stock by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415 of the Securities Act, subject to the terms of the sales agreement. During the three months ended March 31, 2019, the Company sold 119,090 shares of its common stock under the sales agreement at an average price of approximately $13.22 per share for aggregate gross proceeds of approximately $1.6 million and net proceeds of approximately $1.5 million after deducting the sales commissions and offering expenses.

7. Share-Based Compensation

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

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

On March 11, 2019, the Company adopted the 2019 Inducement Equity Incentive Plan (the "2019 Inducement Plan") to reserve 331,500 shares of its common stock to be used exclusively for grants of awards to individuals that were not previously employees or directors of the Company as a material inducement to such individuals' entry into employment with Spero within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. The terms and conditions of the 2019 Inducement Plan are substantially similar to those of the 2017 Plan. As of March 31, 2019, there have been no grants issued under the 2019 Inducement Plan.

As of March 31, 2019, a total of 3,635,225 shares have been authorized and reserved for issuance under all equity plans and 435,488 shares were available for future issuance under such plans.

The following table summarizes stock option activity during the three months ended March 31, 2019:

	Number of Shares
Outstanding as of December 31, 2018	2,297,810
Granted	823,996
Exercised	(10,014)
Forfeited	(28,849)
Outstanding as of March 31, 2019	3,082,943

Included in the options granted above are 100,000 options that contain performance-based vesting criteria, primarily related to the achievement of certain clinical, regulatory and financing milestones. In addition to these stock options, the Company also granted 50,000 restricted stock units ("RSUs") containing the same performance-based vesting criteria. Recognition of stock-based compensation expense associated with these performance-based stock options and RSUs will commence when the performance condition is considered probable of achievement, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

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

	Three Months Ended March 31,	
	2019	2018
Research and development expenses	$ 369	$ 250
General and administrative expenses	564	364
Total	$ 933	$ 614

8. Non-Controlling Interests

Spero Gyrase

As of March 31, 2019 and December 31, 2018, the Company's only remaining non-controlling interest relates to Spero Gyrase, Inc., which totaled $0.4 million. In March 2016, the Company entered into an agreement with Aviragen and its affiliates in order to acquire certain intellectual property and know-how related to certain compounds. In connection with the transaction, the Company established Spero Gyrase, a Delaware corporation, and issued to Aviragen 200 common shares of Spero Gyrase with a fair value of $1.1 million, which represented a 20% equity ownership interest in Spero Gyrase. In addition, Spero Gyrase agreed to make future milestone and royalty payments in exchange for the intellectual property. The Company accounted for the acquisition of technology as an asset acquisition because it did not meet the definition of a business. The Company recorded the acquired technology as research and development expense in the consolidated statement of operations and comprehensive loss in the amount of $1.1 million, because the acquired technology had not reached commercial feasibility and had no alternative future use, and recorded a non-controlling interest in Spero Gyrase in a corresponding amount.

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

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

9. Commitments and Contingencies

License Agreements

The Company has entered into license agreements with various parties under which it is obligated to make contingent and non-contingent payments (see Note 11).

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential

amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company does not believe that the outcome of any claims under indemnification arrangements will have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of March 31, 2019 or December 31, 2018.

Legal Proceedings

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

10. 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 SPR994 for the treatment of complicated urinary tract infections ("cUTI") caused by antibiotic resistant Gram-negative bacteria and for assessment against biodefense pathogens. The award commits initial funding of $15.7 million over a three-year base period from July 1, 2018 to June 30, 2021 for cUTI development activities. The balance of the award is subject to BARDA exercising two options. The exercise of the first option would entail funding of $13.6 million and is exercisable by BARDA subject to the Company achieving specified milestones related to, among other things, clinical progress and data. The exercise of the second option would entail funding of $14.9 million and is exercisable by BARDA subject to, among other things, satisfactory progress and results from the biodefense studies described below. The Company recognized $3.6 million of revenue under this award during the three months ended March 31, 2019.

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

U.S. Department of Defense

In September 2016, the Company was awarded a cooperative agreement with the DoD to further develop anti-infective agents to combat Gram-negative bacteria. The agreement is structured as a single, two-year $1.5 million award. The Company is eligible for the full funding from the DoD, and there are no options to be exercised at a later date. The DoD funding supports next-generation potentiator discovery and screening of SPR741 partners. The Company recognizes revenue under this agreement as qualifying expenses are incurred. The Company recognized less than $0.1 million and $0.1 million of revenue under this agreement during the three months ended March 31, 2019 and 2018, respectively.

NIAID

In February 2017, the Company was awarded a grant from NIAID under its Small Business Innovation Research program, to conduct additional preclinical studies of SPR720, the Company's novel oral bacterial gyrase inhibitor, for the treatment of non-tuberculous mycobacterial infections. The award is structured as a 12-month $0.6 million base period and a $0.4 million option period. Through December 31, 2017, only the base period funds had been committed. In February 2018, NIAID exercised the $0.4 million 12-month option period. In January 2019, the period of performance for this award was extended for an additional 12-month period. The Company recognized $0.3 million and $0.4 million of revenue under this agreement during the three months ended March 31, 2019 and 2018, respectively.

In June 2016, the Company entered into agreements with Pro Bono Bio PLC ("PBB"), a corporation organized under the laws of England, and certain of its affiliates, including PBB Distributions Limited and Ascension Healthcare Development Limited (formerly Cantab Anti-Infectives Limited) ("CAI"), in order to acquire certain intellectual property and government funding arrangements relating to SPR206 (see Note 11). Under these agreements, CAI agreed to submit a request to NIAID to assign the CAI-held NIAID contract to Spero, which was finalized in December 2017. The NIAID contract provides for total development funding of up to $6.3 million, including a base period and three option periods. To date, funding for the base period and the first two option periods totaling $5.7 million have been committed. Spero shall pay PBB a percentage of funds received from NIAID up to a maximum of $1.3

million, of which $0.3 million was paid upfront to PBB as part of this agreement. The Company recorded approximately $0.1 million in expense associated with amounts payable to PBB under this agreement during the three months ended March 31, 2019 and 2018, respectively, which has been included within research and development expenses within the condensed consolidated statement of operations and comprehensive loss.

CARB-X

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

11. Collaboration and License Agreements

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

Aviragen Agreement

Under the Company's agreement with Aviragen (see Note 3) for certain intellectual property and know-how relating to developing a gyrase inhibitor to develop therapies for Gram-negative infections, the Company is obligated to make milestone payments of up to an aggregate of $12.0 million upon the achievement of specified clinical, regulatory and commercial milestones and to pay royalties of low single-digit percentages based on net sales of products the Company acquired under the agreement.

Cantab License Agreement

Under the Cantab Agreements (see Note 10), the Company is obligated to make milestone payments of up to $5.8 million upon the achievement of specified clinical and regulatory milestones and a payment of £5.0 million ($6.5 million and $6.4 million as of March 31, 2019 and December 31, 2018, respectively) upon the achievement of a specified commercial milestone. In addition, the Company has agreed to pay to PBB royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement. During the year ended December 31, 2018, the Company recorded $0.2 million in research and development expense related to the achievement of regulatory milestones for SPR206.

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

Vertex License Agreement

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

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

Meiji License Agreement

In June 2017, the Company entered into agreements with Meiji Seika Pharma Co. Ltd. ("Meiji"), a Japanese corporation, whereby Meiji granted to the Company certain know-how and a license to research, develop, manufacture and sell products for a proprietary compound in the licensed territory. In exchange for the know-how and license, the Company paid Meiji an upfront, one-time, nonrefundable, non-creditable fee of $0.6 million, which was recognized as research and development expense. As part of the agreement, the Company is obligated to make milestone payments of up to $3.0 million upon the achievement of specified clinical and regulatory milestones, to pay royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement and to pay Meiji a low double-digit percentage of any sublicense fees received by the Company up to $7.5 million. In October 2017, the Company paid a $1.0 million milestone payment to Meiji upon the enrollment of the first patient in the Company's Phase 1 clinical trial of SPR994. The payment was recorded as research and development expense in the statement of operations and comprehensive loss for the year ended December 31, 2017. Additionally, 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 condensed consolidated balance sheet.

The agreement continues in effect until the expiration of all payment obligations thereunder (including royalty payments and licensee revenue) on a product-by-product and country-by-country basis, unless earlier terminated by the parties. Pursuant to the terms of the agreement, in addition to each party's right to terminate the agreement upon the other party's material breach (if not cured within a specified period after receipt of notice) or insolvency, the Company also has unilateral termination rights (i) in the event that the Company abandons the development and commercialization of SPR994 for efficacy, safety, legal or business factors, and (ii) under certain circumstances arising out of the head license with a global pharmaceutical company.

Northern License Agreement

In February 2015, the Company's wholly owned subsidiary, Spero Potentiator, issued 996 shares of its common stock with an aggregate fair value of $1.1 million to Northern Antibiotics Oy Ltd. ("Northern") in exchange for an exclusive license to develop and commercialize certain licensed compounds and licensed products. In connection with the acquisition of the license, Northern obtained anti-dilution rights to maintain its 49.9% ownership percentage in Spero Potentiator at no additional cost to Northern in the event that Spero Potentiator completed subsequent equity financings, subject to a maximum amount of such financings. In November 2015, Northern was issued an additional 2,736 common shares of Spero Potentiator for no additional cost as a result of the anti-dilution rights.

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

Everest Medicines License Agreement

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

Under the terms of the Everest License Agreement, the Company received an upfront payment of $3.0 million, comprised of a $2.0 million payment to license SPR206 and $1.0 million for the exclusive option to negotiate a license to develop SPR741. The Company will receive a milestone payment of $2.0 million upon completion and delivery of the results of a clinical study and future milestones of up to $1.5 million if the Company chooses to complete a future clinical study. The Company may also receive up to an additional $55.0 million in milestone payments upon Everest's achievement of certain developmental, regulatory and sales milestone

events related to SPR206, which achievement cannot be guaranteed. The Company is also entitled to receive high single-digit to low double-digit royalties on net sales, if any, of Licensed Products in the Territory following regulatory approval of SPR206. Everest has the right to sublicense to affiliates and third parties in the Territory.

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

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

Accounting Analysis and Revenue Recognition

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

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

Performance Obligations	Standalone Selling Price	Transaction Price Allocated	Recognition Method
License and know-how transfer (1)	$ 9,858	$ 3,553	Fully satisfied; recognized upon delivery of the license
Exclusive option on SPR741	400	144	Will be recognized upon exercise or expiration of the option
Research and development services (2)	3,614	1,303	Recognized over time as services are delivered through the expected completion date of Q1 2020
		$ 5,000	

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

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

During the three months ended March 31, 2019, the Company recognized $3.8 million of revenue related to this agreement. As of March 31, 2019, the aggregate amount of the transaction price allocated to performance obligations that are partially unsatisfied was $1.2 million. The Company has a contract asset of $0.8 million, which is included in prepaid expenses and other current assets in the condensed consolidated balance sheet as of March 31, 2019.

12. Australia Research and Development Tax Incentive

The Australian government has established a research and development tax incentive to encourage industry investment in research and development, which is available to companies incorporated under Australian law that have core research and development activities. In September 2016, the Company established Spero Potentiator Australia Pty Limited to carry out certain

research and development activities. As this subsidiary meets the eligibility requirements of the Australian tax law, it is eligible to receive a 43.5% tax incentive for qualified research and development activities. The Company recorded less than $0.1 million as a reduction to research and development expenses in the consolidated statements of operations and comprehensive loss during both the three months ended March 31, 2019 and 2018, respectively, associated with this tax incentive, representing 43.5% of the Company's qualified research and development spending in Australia. The tax incentive refund is denominated in Australian dollars and, therefore, the associated tax incentive receivable is re-measured to U.S. dollars as of each reporting date. The Company's tax incentive receivables from the Australian government totaled $1.2 million and $1.1 million as of March 31, 2019, and December 31, 2018, respectively.

13. Net Loss per Share

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

	Three Months Ended March 31,	
	2019	2018
Numerator:		
Net loss	$ (5,072)	$ (10,644)
Denominator:		
Weighted average common shares outstanding, basic and diluted	17,221,120	14,369,182
Net loss per share, basic and diluted	$ (0.29)	$ (0.74)

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

	Three Months Ended March 31,	
	2019	2018
Options to purchase common stock	3,082,943	2,129,082
Unvested restricted stock units	50,000	—
Series A convertible preferred stock (as converted to common shares)	2,220,000	—
Series B convertible preferred stock (as converted to common shares)	1,000,000	—
	6,352,943	2,129,082

14. Subsequent Events

The Company has evaluated, for potential recognition and disclosure, events that occurred prior to the date at which the condensed consolidated financial statements were available to be issued. Other than as disclosed below, there were no material subsequent events.

Subsequent to March 31, 2019, the Company sold 198,924 shares of its common stock under the at-the-market offering program sales agreement with Cantor at an average price of approximately $12.84 per share for aggregate gross proceeds of approximately $2.6 million prior to deducting sales commissions and offering expenses.

Item 2. 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 the unaudited financial information and the notes thereto included appearing elsewhere in this Quarterly Report on Form 10-Q, and the audited financial information and the notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2018. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, 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 Quarterly Report on Form 10-Q, our actual results could differ materially from the results described in, or implied by, the forward-looking statements contained in the following discussion and analysis.

Overview

We are a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing and commercializing novel treatments for multi-drug resistant bacterial infections. Our most advanced product candidate, SPR994 (tebipenem pivoxil hydrobromide), is designed to be the first broad-spectrum oral carbapenem-class antibiotic for use in adults to treat multi-drug resistant, or MDR, Gram-negative infections. Treatment with effective orally administrable antibiotics may prevent hospitalizations for serious infections and enable earlier, more convenient and cost-effective treatment of patients after hospitalization. We are also developing SPR720, an oral antibiotic designed for the treatment of pulmonary non-tuberculous mycobacterial infection, or NTM, infection. In addition, we also have a platform technology known as our Potentiator Platform, which includes two IV-administered agents, SPR206 and SPR741, that are active either alone or in combination with other standard of care agents and are designed to treat MDR Gram-negative bacteria in the hospital. We believe that our novel product candidates, if successfully developed and approved, would have a meaningful patient impact and significant commercial applications for the treatment of MDR infections in both the community and hospital settings. Since our inception in 2013, we have focused substantially all of our efforts and financial resources on organizing and staffing our company, business planning, raising capital, acquiring and developing product and technology rights, building our intellectual property portfolio and conducting research and development activities for our product candidates. We do not have any products approved for sale and have not generated any revenue from product sales.

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

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

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

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

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

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

Prior to the IPO and our July 2018 equity offering, we funded our operations with proceeds from the sale of preferred units and bridge units and payments received under a concluded collaboration agreement and funding from government contracts. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. As of March 31, 2019, we had an accumulated deficit of $143.6 million. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years.

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

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

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

As of March 31, 2019, we had cash, cash equivalents and marketable securities of $106.4 million. We believe that our existing cash, cash equivalents and marketable securities, together with the initial funding committed under our BARDA award in July 2018, will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2020, including through top-line data readout of our pivotal Phase 3 clinical trial of SPR994. As described elsewhere, a portion of the funding from our BARDA award supporting the development of SPR994 is scheduled to occur in periods after 2020, provided we achieve specified milestones under the award agreement and BARDA exercises all of its options under the agreement.

Recent Developments

SPR994 Pivotal Phase 3 Trial Initiated

In January 2019 we announced the receipt of positive feedback from the U.S. Food and Drug Administration, or FDA, from our pre-Phase 3 meeting. As a result of the meeting, we submitted an IND application for SPR994 in complicated urinary tract infections, or cUTI, with the U.S. Food and Drug Administration, or FDA. In February 2019 we received FDA acceptance of our investigational new drug, or IND, application for SPR994 in cUTI. We opened clinical trial sites in April 2019, and the patient screening period for our SPR994 pivotal Phase 3 trial has begun. The Phase 3 trial, ADAPT-PO, is a randomized, double-blind, double-dummy, multicenter study to assess SPR994 at a dose of 600 mg administered three times per day versus intravenous Ertapenem in patients with cUTI or acute pyelonephritis.

SPR994 Granted Fast Track Designation by the FDA for the treatment of Complicated Urinary Tract infections and Acute Pyelonephritis

In March 2019, we announced that the FDA had granted Fast Track Designation for SPR994, for the treatment of complicated urinary tract infections and acute pyelonephritis. The FDA's Fast Track program facilitates development and expedites review of drugs intended to treat serious or life-threatening conditions that demonstrate the potential to address unmet medical needs. Fast Track Designation provides opportunities for more frequent interaction with the FDA review team to expedite development and review as well as provides an opportunity for rolling review of the new drug application, or NDA, upon request and agreement with the FDA. In addition, the Fast Track program allows for eligibility for Accelerated Approval and Priority Review, if relevant criteria are met. In addition to Fast Track Designation, SPR994 was previously granted Qualified Infectious Disease Product designation, or QIDP,

designation. SPR994 will receive FDA priority review of the first marketing application or efficacy supplement for SPR994 and the indication for which QIDP designation was granted.

SPR206 license agreement with Everest Medicines

On January 4, 2019, the Company, through our wholly owned subsidiary NPLH, entered into a license agreement with Everest Medicines II Limited whereby we granted Everest an exclusive license to develop, manufacture and commercialize SPR206, or products containing SPR206, in Greater China, South Korea and certain Southeast Asian countries. We retained development, manufacturing and commercialization rights with respect to SPR206 and Licensed Products in the rest of the world and also retained the right to develop or manufacture SPR206 and Licensed Products in the Territory for use outside the Territory. In addition to the license grant with respect to SPR206, we also granted to Everest a 12-month exclusive option to negotiate with us for an exclusive license to develop, manufacture or commercialize SPR741 in the same territories. We received from Everest an upfront payment of $3.0 million and are eligible to receive milestone payments of up to an additional $58.5 million upon Everest's achievement of specified clinical, regulatory and commercial milestones related to SPR206, of which we anticipate receiving at least $2.0 million in near-term milestones during 2019. Furthermore, we are eligible to receive high single-digit to low double-digit royalties on net sales of products containing SPR206 in the covered territories following regulatory approval of SPR206.

Components of Our Results of Operations

Grant Revenue

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

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

BARDA

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

U.S. Department of Defense

In September 2016, we were awarded a cooperative agreement with the U.S. Department of Defense to further develop anti-infective agents to combat Gram-negative bacteria. The agreement is structured as a single, two-year $1.5 million award. We are eligible for the full funding from DoD and there are no options to be exercised at a later date. The DoD funding supports next-generation potentiator discovery and screening of SPR741 partner antibiotics. We receive funding under the DoD award as we incur qualifying expenses.

NIAID

In February 2017, we received an award from the U.S. National Institute of Allergy and Infectious Diseases under its Small Business Innovation Research program to conduct additional preclinical studies of SPR720. The award is structured as a 12-month $0.6 million base period, which has already been committed, and a $0.4 million option period. In February 2018 NIAID exercised the $0.4 million 12-month option period. In January 2019, the period of performance for this award was extended for an additional 12-month period, through February 2020. We receive funding under the NIAID award as we incur qualifying expenses.

In June 2016, we entered into agreements with Pro Bono Bio PLC, a corporation organized under the laws of England, and certain of its affiliates, including PBB Distributions Limited and Ascension Healthcare Development Limited (formerly Cantab Anti-Infectives Limited), or CAI, in order to acquire certain intellectual property and government funding arrangements relating to SPR206.

Under these agreements, CAI agreed to submit a request to NIAID to assign the then CAI-held NIAID contract to us. Novation of the NIAID contract was finalized in December 2017. The NIAID contract provides for development funding of up to $6.3 million over a base period and three option periods. To date, funding for the base period and the first two option periods totaling $5.7 million have been committed. We will pay PBB a percentage of funds received from NIAID up to a maximum of $1.3 million of which $0.3 million was paid upfront to PBB as part of this agreement. During the year ended December 31, 2018, we recorded approximately $0.4 million in expense related to amounts payable to PBB under this agreement. During the three months ended March 31, 2019 we recorded approximately $0.1 million in expense related to amounts payable to PBB under this agreement.

CARB-X

In April 2017, we received an award from the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, a public-private partnership funded by the BARDA within the U.S. Department of Health and Human Services, to be used to screen, identify and complete Phase 1 clinical trials with at least one partner compound for SPR741. The award committed funding of $1.5 million over a 12-month period. On March 12, 2018, CARB-X committed an additional $0.4 million related to the first option for a period from December 1, 2017 to March 31, 2018. There will be no additional options exercised under the CARB-X award.

Collaboration Revenue

Collaboration revenue relates to our agreement with Everest Medicines.

Operating Expenses

Research and Development Expenses

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

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

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

Since the fourth quarter of 2016 and through March 31, 2019, we have recorded research and development expenses conducted by our Australian subsidiary net of a 43.5% research and development tax incentive we expect to receive for qualified expenses from the Australian government.

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

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

associated with our preclinical programs or facility expenses, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple product development programs and, as such, are not separately classified. The table below summarizes our research and development expenses incurred by development program (in thousands):

	Three Months Ended March 31,		
	2019	2018	$ Change
Direct research and development expenses by program:			
SPR994	$ 3,708	$ 2,352	$ 1,356
SPR720	1,064	364	700
Potentiator Platform (SPR206 and SPR741)	1,236	3,441	(2,205)
Preclinical programs	—	31	(31)
Unallocated expenses:			
Personnel related (including share-based compensation)	2,582	1,831	751
Facility related and other	936	906	30
Total research and development expenses	$ 9,526	$ 8,925	$ 601

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will increase substantially in connection with our planned clinical development activities in the near term and in the future as we progress our existing clinical trials and other studies of SPR994, SPR720 and SPR206, continue to discover and develop additional product candidates, hire additional clinical and scientific personnel and acquire or in-license other product candidates and technologies.

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

- successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers to obtain manufacturing supply;
- obtainment and maintenance of patent, trade secret protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain our license agreement with Meiji with respect to SPR994;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales of SPR994 and our other product candidates, if approved, whether alone or in collaboration with others;
- acceptance of SPR994 and our other product candidates, if approved, by patients, the medical community and third-party payors;
- competition with other therapies; and
- a continued acceptable safety profile of SPR994 and our other product candidates, if approved.

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

General and Administrative Expenses

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

increased accounting, audit, legal, regulatory, compliance, and director and officer insurance costs as well as investor and public relations expenses associated with operating as a public company.

Other Income (Expense)

Interest Income and Other Income (Expense), Net

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

Income Taxes

Since our inception, we have not recorded any income tax benefits for the net losses we have incurred in each year or for our earned research and development tax credits, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating loss carryforwards and tax credits will not be realized. As of December 31, 2018, we had federal and state net operating loss carryforwards of $100.4 million and $100.3 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2033. In addition, as of December 31, 2018, we had foreign net operating loss carryforwards of $11.7 million, which may be available to offset future income tax liabilities and do not expire. As of December 31, 2018, we also had federal and state research and development tax credit carryforwards of $2.6 million and $0.8 million, respectively, which begin to expire in 2033 and 2028, respectively. We have recorded a full valuation allowance against our net deferred tax assets at each balance sheet date.

Results of Operations

Comparison of the Three Months Ended March 31, 2019 and 2018

The following table summarizes our results of operations for the three months ended March 31, 2019 and 2018 (in thousands):

	Three Months Ended March 31,		
	2019	2018	$ Change
Revenues:			
Grant revenue	$ 3,911	$ 1,153	$ 2,758
Collaboration revenue	3,807	—	3,807
Total revenues	7,718	1,153	6,565
Operating expenses:			
Research and development	9,526	8,925	601
General and administrative	3,888	3,044	844
Total operating expenses	13,414	11,969	1,445
Loss from operations	(5,696)	(10,816)	5,120
Other income (expense):			
Interest income and other income (expense), net	624	172	452
Total other income (expense), net	624	172	452
Net loss	$ (5,072)	$ (10,644)	$ 5,572

Grant Revenue

	Three Months Ended March 31,		
	2019	2018	$ Change
BARDA Contract (SPR994)	$ 3,599	$ —	$ 3,599
NIAID Contract (SPR206)	279	390	(111)
NIAID Award (SPR720)	31	156	(125)
DoD Agreement (Potentiator Platform)	2	112	(110)
CARB-X Award (SPR741)	—	495	(495)
Total grant revenue	$ 3,911	$ 1,153	$ 2,758

Grant revenue recognized during the three months ended March 31, 2019 and 2018 consisted of the reimbursement of qualifying expenses incurred in connection with our various government awards. The increase in revenue during the three months ended March 31, 2019 was primarily due to funding received under our BARDA contract, which was awarded to us in July 2018, and for which we began incurring qualified expenses in the second half of 2018, as well as the NIAID contract, which provides funding for SPR206, which was novated to us from CAI in December 2017. Offsetting these increases, were decreases in funding received under our DoD agreement, as well as our CARB-X award, which had a performance period through March 31, 2018.

Collaboration Revenue

During the three months ended March 31, 2019, we recognized $3.8 million of revenue related to our agreement with Everest Medicines, consisting of the delivery of the license and the performance of research and development services.

Research and Development Expenses

	Three Months Ended March 31,		
	2019	2018	$ Change
Direct research and development expenses by program:			
SPR994	$ 3,708	$ 2,352	$ 1,356
SPR720	1,064	364	700
Potentiator Platform (SPR206 and SPR741)	1,236	3,441	(2,205)
Preclinical programs	—	31	(31)
Unallocated expenses:			
Personnel related (including share-based compensation)	2,582	1,831	751
Facility related and other	936	906	30
Total research and development expenses	$ 9,526	$ 8,925	$ 601

Direct costs related to our SPR994 program increased during the three months ended March 31, 2019 compared to the three months ended March 31, 2018 due to costs related to our pivotal Phase 3 clinical trial, partially offset by a decrease in expenses related to formulation development, manufacturing process and manufacturing of clinical trial material.

Direct costs related to our SPR720 program increased during the three months ended March 31, 2019 as compared to the three months ended March 31, 2018, primarily related to costs incurred to prepare for the Phase 1 clinical trial of SPR720, which we initiated in January 2019.

Direct costs related to our Potentiator Platform include costs related to our SPR206 and SPR741 programs. Direct costs related to our SPR206 program decreased by $1.4 million during the three months ended March 31, 2019, primarily due to higher preclinical costs incurred in the prior year. Direct costs related to our SPR741 program decreased by $0.8 million during 2018, primarily due to the completion of our Phase 1b drug-drug interaction clinical trial of SPR741 in the United Kingdom during the first half of 2018.

Direct costs related to our preclinical programs decreased during the three months ended March 31, 2019 compared to the three months ended March 31, 2018 due primarily to lower spending on preclinical programs as we focused development efforts on our product candidates.

The increase in personnel-related costs included in unallocated expenses was due to an increase in headcount in our research and development function. Personnel-related costs for the three months ended March 31, 2019 and 2018 included share-based compensation expense of $0.4 million and $0.3 million, respectively.

General and Administrative Expenses

	Three Months Ended March 31,		
	2019	2018	$ Change
Personnel related (including share-based compensation)	$ 2,003	$ 1,507	$ 496
Professional and consultant fees	1,371	1,309	62
Facility related and other	514	228	286
Total general and administrative expenses	$ 3,888	$ 3,044	$ 844

The increase in personnel-related costs of $0.5 million was primarily a result of an increase in headcount in our general and administrative function. Personnel-related costs for the three months ended March 31, 2019 and 2018 included share-based compensation expense of $0.6 million and $0.4 million, respectively.

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

Other Income (Expense), Net

Other income, net was $0.6 million for the three months ended March 31, 2019, compared to $0.2 million for the three months ended March 31, 2018 and was primarily comprised of interest earned on invested cash balances and marketable securities.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We have generated limited revenue to date from funding arrangements with the DoD, NIAID, CARB-X and BARDA. We have not yet commercialized any of our product candidates and we do not expect to generate revenue from sales of any product candidates for several years, if at all. To date, we have funded our operations with proceeds from the sales of preferred units and bridge units, payments received under a concluded collaboration agreement and funding from government contracts, with proceeds from the IPO of our common stock, and in July 2018 with an underwritten public offering of our common and preferred stock, and subsequent sales of our common stock. As of March 31, 2019, we had cash, cash equivalents and marketable securities of $106.4 million.

On December 3, 2018, we filed a universal shelf registration statement on Form S-3 (Registration No. 333-228661) with the SEC, which was declared effective on December 11, 2018, and pursuant to which we registered for sale up to $200.0 million of any combination of our common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that we may determine, including up to $50.0 million of our common stock available for issuance pursuant to an at-the-market offering program sales agreement that we entered into with Cantor Fitzgerald & Co. Under the sales agreement, Cantor may sell shares of our common stock by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415 of the Securities Act, subject to the terms of the sales agreement. During the three months ended March 31, 2019 we sold 119,090 shares of common stock under the sales agreement at an average price of approximately $13.22 per share for aggregate gross proceeds of $1.6 million and net proceeds of $1.5 million after deducting the sales commissions and offering expenses.

Subsequent to March 31, 2019, we sold 198,924 shares of common stock under the at-the-market offering program sales agreement with Cantor at an average price of approximately $12.84 per share for aggregate gross proceeds of approximately $2.6 million prior to deducting sales commissions and offering expenses.

Cash Flows

The following table summarizes our sources and uses of cash for the three months ended March 31, 2019 and 2018:

	Three Months Ended March 31,	
	2019	2018
Cash used in operating activities	$ (10,924)	$ (11,961)
Cash provided by (used in) investing activities	24,671	(22,825)
Cash provided by financing activities	1,568	—
Net increase (decrease) in cash and cash equivalents	$ 15,315	$ (34,786)

Operating Activities

Net cash used in operating activities for the three months ended March 31, 2019 was $10.9 million, primarily resulting from our net loss of $5.1 million, adjusted for net non-cash items of $0.7 million (primarily stock-based compensation). Net cash provided by changes in our operating assets and liabilities was $6.5 million and consisted primarily of a $6.4 million decrease in accounts payable and accrued expenses, a $0.4 million increase in prepaid expenses and other current assets, a $0.4 million increase in other assets, and an increase of $0.1 million in receivables related to the Australian research and development tax initiative and our receivables under our government awards.

Net cash used in operating activities for the three months ended March 31, 2018 was $12.0 million, primarily resulting from our net loss of $10.6 million, adjusted for net non-cash items of $0.7 million (primarily stock-based compensation). Net cash used by

changes in our operating assets and liabilities was $2.0 million and consisted primarily of a decrease of $2.3 million in accounts payable and accrued expenses, partially offset by an increase of $0.3 million in other receivables.

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

Investing Activities

Cash provided by investing activities during the three months ended March 31, 2019 was $24.7 million primarily related to the net maturities of marketable securities. Cash used in investing activities during the three months ended March 31, 2018 was $22.8 million related to the purchase of marketable securities.

Financing Activities

Cash used in financing activities during the three months ended March 31, 2019, of $1.6 million consisted primarily of proceeds of $1.5 million from the sale of common stock under our at-the-market offering program sales agreement as well as less than $0.1 million of proceeds from the exercise of employee stock options.

Funding Requirements

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

- the timing and costs of our planned clinical trials;
- the initiation, progress, timing, costs and results of preclinical studies and clinical trials of our other product candidates and potential new product candidates;
- the amount of funding that we receive under government contracts that we have applied for;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for SPR994 and other product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the receipt of marketing approval and revenue received from any potential commercial sales of SPR994;
- the terms and timing of any future collaborations, licensing or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to our license agreements;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;
- the costs of operating as a public company; and
- the extent to which we in-license or acquire other products and technologies.

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

We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization

of pharmaceutical product candidates, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements will depend on and could increase significantly as a result of many factors, including those listed above.

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

Contractual Obligations and Commitments

During the three months ended March 31, 2019, there have been no material changes to our contractual obligations and commitments outside the ordinary course of business from those described under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations—Contractual Obligations and Commitments" in our Annual Report on Form 10-K for the year ended December 31, 2018.

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of our consolidated financial statements and related disclosures requires us to make estimates, assumptions and judgments that affect the reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

We believe that of our critical accounting policies described under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations–Critical Accounting Policies and Significant Judgments and Estimates" in our Annual Report on Form 10-K for the year ended December 31, 2018, the following accounting policies involve the most judgement and complexity:

- revenue recognition for funding received from government contracts, tax incentives and collaborations;
- accrued research and development expenses; and
- share-based compensation.

Accordingly, we believe the policies set forth above are critical to fully understanding and evaluating our financial condition and results of operations. If actual results or events differ materially from the estimates, judgments and assumptions used by us in applying these policies, our reported financial condition and results of operations could be materially affected. There have been no material changes to our critical accounting policies since December 31, 2018, except as noted below with respect to our accounting for revenue under Accounting Standards Codification, or ASC, Topic 606.

Revenue Recognition – Collaboration Revenue

Effective January 1, 2019, we entered into a licensing agreement that is evaluated under Accounting Standards Codification, Topic 606 ("Topic 606"), *Revenue from Contracts with Customers*, through which we license certain of our product candidates' rights to a third party. Any future out-licensing agreements entered into by us and additional third parties shall also be evaluated under Topic 606. 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 any 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. We only apply the five-step model to contracts when it is probable that we will collect the consideration to which we are entitled in exchange for the goods or services we transfer to a customer.

Once a contract is determined to be within the scope of Topic 606, we assess the goods or services promised within each contract and determine 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. We assess 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.

We assess 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, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. We also consider 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, we are 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. 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, we consider 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, we 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. We validate 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, we estimate the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. We determine the amount of variable consideration by using the expected value method or the most likely amount method. We include 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, we re-evaluate 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, we evaluate 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 our 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, we adjust consideration for the effects of the time value of money if the timing of payments provides us with a significant benefit of financing. We do 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. We assessed its revenue-generating arrangement in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in the arrangement. 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, we recognize 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.

We then recognize 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.

To determine the amount and timing of revenue to be recognized under each agreement, we evaluate the following criteria: (i) confirming the goods or services in the contract; (ii) defining the performance obligations under the agreement; (iii) determining the transaction price, including any constraint on variable consideration; (iv) allocating the transaction price to the performance obligations; and (v) defining how the revenue will be recognized for each performance obligation. In determining the accounting treatment for these arrangements, we develop assumptions to determine the stand-alone selling price for each performance obligation in the contract. These assumptions may include forecasted revenues, development timelines, discount rates and probabilities of technical and regulatory success.

Off-Balance Sheet Arrangements

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

Recently Issued and Adopted Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

As of March 31, 2019, we had cash, cash equivalents and marketable securities of $106.4 million, consisting of cash, corporate bonds, commercial paper, money market accounts and U.S. government debt securities. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. If market interest rates were to increase immediately and uniformly by 50 basis points, from levels as of March 31, 2019, the net fair value of our interest sensitive marketable securities would hypothetically decline by approximately $0.1 million. As we incur research expenses in foreign countries, we face exposure to movements in foreign currency exchange rates, primarily the Euro, British Pound and Australian dollar against the U.S. dollar. Historically, foreign currency fluctuations have not had a material impact on our consolidated financial statements.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

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

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 March 31, 2019 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. We implemented internal controls to ensure management properly assessed the impact of the new lease accounting standards on our condensed consolidated financial statements to facilitate adoption of the new leasing standards effective January 1, 2019. There were no significant changes to our internal control over financial reporting due to the adoption of the new standards.

PART II—OTHER INFORMATION

Item 1A. Risk Factors.

Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Quarterly Report, including the section of this Quarterly Report titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes, and in other documents that we file with the SEC, in evaluating our company and our business. Investing in our securities involves a high degree of risk. If any of the events described in the following risk factors 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 Quarterly Report on Form 10-Q.

Risks Related to Our Financial Position and Need for Additional Capital

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

We are a clinical-stage biopharmaceutical company with a limited operating history. We have not generated any revenue from the sale of products and have incurred losses in each year since our inception in 2013. Our net loss was $5.1 million and $10.6 million for the three months ended March 31, 2019 and 2018, respectively. All of our product candidates are in development, none have been approved for sale and we may never have a product candidate approved for commercialization. We have financed our operations primarily through sales of our equity securities, collaborations and government funding for research and development. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical and clinical development.

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

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

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

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

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

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete. We expect that our expenses will increase substantially as we commence and advance our ongoing and planned clinical trials and other studies of SPR994, SPR720 and SPR206, seek marketing approval for SPR994 if clinical trials are successful, and evaluate the advancement of our other product candidates. If we obtain marketing approval for SPR994 or any other product candidate, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Some of these expenses may be incurred in advance of marketing approval, and could be substantial. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations, licensing arrangements, government funding or other sources. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to pursue our business strategy.

We believe that our existing cash, cash equivalents and marketable securities as of March 31, 2019, together with the initial funding committed under our BARDA award in July 2018, will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2020, including through the top-line readout of our pivotal Phase 3 clinical trial of SPR994. Our cash forecasts are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the timing, costs and results of our ongoing and planned clinical trials of SPR994;
- the timing, costs and results of our ongoing, planned and potential clinical trials for other product candidates;
- the amount of funding that we receive under our government awards;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for SPR994 and other product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the receipt of marketing approval and revenue received from any potential commercial sales of SPR994;
- the terms and timing of any future collaborations, licensing or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to our license agreements;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;
- the costs of operating as a public company; and
- the extent to which we in-license or acquire other products and technologies.

As of March 31, 2019, our non-dilutive sources of funding consisted of an award from BARDA for SPR994, an award from NIAID under its Small Business Innovation Research program or SBIR, for our SPR720 program, an award from NIAID for SPR206, and awards from CARB-X and the DoD that provide partial funding for the development of our Potentiator Platform product candidates.

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

The NIAID contract for SPR206 provides for total development funding of up to $6.3 million over a base period and three option periods. To date, funding for the base period and the first two option periods totaling $5.7 million have been committed. The NIAID SBIR award is structured as a base period followed by a single option. For the base period of March 1, 2017 through February 28, 2018, NIAID committed funding of approximately $0.6 million for the SPR720 program. In February 2018 NIAID exercised the approximately $0.4 million option, which will have a period of performance from March 1, 2018 through February 28, 2019. In January 2019, the period of performance for this award was extended for an additional 12-month period. Our DoD cooperative agreement is structured as a single, two-year $1.5 million award. We are eligible for the full funding from the DoD and there are no options to be exercised at a later date. The CARB-X award is structured as a base period followed by two sequential options. In March 2017, CARB-X committed funds of $1.5 million to support SPR741 development efforts for the period from April 1, 2017 to March 31, 2018. On March 12, 2018, CARB-X committed an additional $0.4 million related to the first option for a period from December 1, 2017 to March 31, 2018. There will be no additional options exercised under the CARB-X award. The NIAID award is subject to termination for convenience at any time by NIAID. NIAID is not obligated to provide funding to Spero beyond the base period amounts from Congressionally approved annual appropriations.

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

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

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

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

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

As of December 31, 2018, we had U.S. federal, state and foreign net operating loss carryforwards, or NOLs, of $100.4 million, $100.3 million and $11.7 million, respectively. Our NOLs begin to expire in 2033. Utilization of these NOLs depends on many factors, including our future income, which cannot be assured. These NOLs could expire unused and be unavailable to offset our future income tax liabilities. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership by 5% stockholders over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes to offset its post-change income may be limited. We have not determined if we have experienced Section 382 ownership changes in the past and if a portion of our NOLs is subject to an annual limitation under Section 382. In addition, we may experience ownership changes in the future as a result of subsequent changes in our stock ownership, some of which may be outside of our control. If we determine that an ownership change has occurred and our ability to use our historical NOLs is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

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

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

We were established in 2013 and began operations in 2014. Our operations to date have been limited to financing and staffing our company, developing our technology and developing SPR994 and our other product candidates. We have not yet demonstrated an ability to successfully complete a large-scale, pivotal clinical trial, obtain marketing approval, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

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

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

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

Risks Related to Product Development and Commercialization

We are heavily dependent on the success of SPR994, which is still under development, and our ability to develop, obtain marketing approval for and successfully commercialize SPR994. If we are unable to develop, obtain marketing approval for and successfully commercialize SPR994, or if we experience significant delays in doing so, our business could be materially harmed.

We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of SPR994 as a product candidate for the treatment of MDR bacterial infections. Our near-term prospects are substantially dependent on our ability to develop, obtain marketing approval for and successfully commercialize SPR994. The success of SPR994 will depend on several factors, including the following:

- successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers to obtain manufacturing supply;
- obtainment and maintenance of patent, trade secret protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain our license agreement with Meiji with respect to SPR994;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales of SPR994, if approved, whether alone or in collaboration with others;
- acceptance of SPR994, if approved, by patients, the medical community and third-party payors;
- competition with other therapies; and
- a continued acceptable safety profile of SPR994 following approval.

Successful development of SPR994 for any additional indications would be subject to these same risks.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to develop, receive marketing approval for, or successfully commercialize SPR994, or if we experience delays as a result of any of these factors or otherwise, our business could be materially harmed.

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

As a company, we have never obtained regulatory approval for, or commercialized, a drug. It is possible that the FDA may refuse to accept any or all of our planned new drug applications, or NDAs, for substantive review or may conclude after review of our data that our application is insufficient to obtain regulatory approval for any current or future product candidates. If the FDA does not approve any of our planned NDAs, it may require that we conduct additional costly clinical, nonclinical or manufacturing validation

studies before it will reconsider our applications. Depending on the extent of these or any other FDA-required studies, approval of any NDA or other application that we submit may be significantly delayed, possibly for several years, or may require us to expend more resources than we have available. Any failure or delay in obtaining regulatory approvals would prevent us from commercializing SPR994 or any of our other product candidates for which we may seek regulatory approval, generating revenues and achieving and sustaining profitability. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve any NDA or other application that we submit. If any of these outcomes occur, we may be forced to abandon the development of our product candidates, which would materially adversely affect our business and could potentially cause us to cease operations. We face similar risks for our applications in foreign jurisdictions.

If clinical trials of SPR994 or any other product candidate that we may advance to clinical trials fail to demonstrate safety and efficacy to the satisfaction of the FDA or comparable foreign regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of SPR994 or any other product candidate.

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

The clinical development of SPR994 and any of our other product candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to demonstrate efficacy in a trial or across a broad population of patients, the occurrence of severe adverse events, failure to comply with protocols or applicable regulatory requirements, and determination by the FDA or any comparable foreign regulatory authority that a drug product is not approvable. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in clinical trials, even after promising results in earlier nonclinical studies or clinical trials. The results of preclinical and other nonclinical studies and/or early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Notwithstanding any promising results in early nonclinical studies or clinical trials, we cannot be certain that we will not face similar setbacks. For example, although SPR994 is a new formulation of the active pharmaceutical ingredient tebipenem that exhibited a favorable safety and efficacy profile during clinical trials conducted by Meiji and a global pharmaceutical company, which we refer to as Global Pharma, in Japan, we may nonetheless fail to achieve success in our clinical trials. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates.

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

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

We may encounter unforeseen events prior to, during, or as a result of, clinical trials that could delay or prevent us from obtaining regulatory approval for SPR994 or any of our other product candidates, including:

- the FDA or other comparable foreign regulatory authorities may disagree as to the design or implementation of our clinical trials;
- we may not reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of our product candidates may produce unfavorable or inconclusive results;

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

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

If we are required to conduct additional clinical trials or other testing of SPR994 or any other product candidate beyond the trials and testing that we contemplate, if we are unable to successfully complete clinical trials or other testing of our product candidates, if the results of these trials or tests are unfavorable or are only modestly favorable or if there are safety concerns associated with SPR994 or any other product candidate, we may:

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

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

which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of SPR994 or any other product candidate.

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

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. We may not be able to initiate, continue or complete clinical trials of SPR994 or any other product candidate that we develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials as required by the FDA or comparable foreign regulatory authorities, such as the EMA. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

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

The inclusion and exclusion criteria for our contemplated Phase 3 clinical trial of SPR994 may adversely affect our enrollment rates for patients in these trials. In addition, many of our competitors also have ongoing clinical trials for product candidates that would treat the same indications as we contemplate for SPR994 or our other product candidates, and patients who would otherwise be eligible for any clinical trials we may conduct for such product candidates may instead enroll in clinical trials of our competitors' product candidates.

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

Future legislation, and/or regulations and policies adopted by the FDA, the EMA or similar regulatory authorities may increase the time and cost required for us to conduct and complete clinical trials of SPR994 and our other product candidates and potential product candidates.

The FDA has established regulations to govern the drug development and approval process, as have foreign regulatory authorities. The policies of the FDA and other regulatory authorities may change and additional laws may be enacted or government regulations may be promulgated that could prevent, limit, delay but also accelerate regulatory review of our product candidates. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but all of its provisions have not yet been implemented. Among other things, the Cures Act provides a new "limited population" pathway for certain antibacterial and antifungal drugs, or LPAD, but the FDA has not yet issued guidance regarding the LPAD. Additionally, in August 2017, FDA issued final guidance setting forth its current thinking with respect to development programs and clinical trial designs for antibacterial drugs to treat serious bacterial diseases in patients with an unmet medical need. We cannot predict what if any effect the Cures Act or any existing or future guidance from FDA will have on the development of our product candidates.

Our clinical program for SPR994 is subject to a number of specific risks that may affect the outcome of the trial, including the use of a new formulation of the active pharmaceutical ingredient, tebipenem.

Our pivotal Phase 3 clinical trial of SPR994 is subject to a number of specific risks arising from our clinical program and the design of the trial. We have not conducted a clinical trial of SPR994 in patients with cUTI, who will be the subjects of the clinical trial, and we have no direct clinical evidence that SPR994 is effective in treating cUTIs in humans. Although we believe that SPR994

has the potential to treat cUTI in humans based on the results of our nonclinical *in vitro* and *in vivo* animal model studies, together with Meiji's and Global Pharma's Phase 2 clinical trial results, these results are not necessarily predictive of the results of our planned clinical trials and we cannot guarantee that SPR994 will demonstrate the expected efficacy in our pivotal Phase 3 clinical trial patients. We also cannot guarantee that the projections made from the pharmacokinetic and pharmacodynamic models that we developed from our nonclinical and clinical SPR994 studies will be validated in our pivotal Phase 3 clinical trial.

In addition, we may face competition in enrolling suitable patients as a result of other companies conducting clinical trials for antibiotic product candidates that are intended to treat similar infections, resulting in slower than anticipated enrollment in our trials. Enrollment delays in the trial may result in increased development costs for SPR994, or slow down or halt our product development for SPR994.

To support our accelerated clinical development strategy for SPR994, we are relying, in part, on clinical data from two exploratory Phase 2 clinical trials conducted by Meiji (ME1211) and Global Pharma (L-084 04) in Japan, which were not conducted in accordance with FDA guidance for clinical trials in patients with cUTI. To the extent that these clinical trial design differences limit our use of the clinical data, our proposed clinical trial plan for SPR994 with the FDA could be materially delayed and we may incur material additional costs.

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

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

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

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

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

Serious adverse events or undesirable side effects or other unexpected properties of SPR994 or any other product candidate may be identified during development or after approval that could delay, prevent or cause the withdrawal of regulatory approval, limit the commercial potential, or result in significant negative consequences following marketing approval.

Serious adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, an institutional review board, or regulatory authorities to interrupt, delay or halt our clinical trials and could result in a more restrictive label, the imposition of distribution or use restrictions or the delay or denial of regulatory approval by the FDA or

comparable foreign regulatory authorities. If SPR994 or any of our other product candidates is associated with serious or unexpected adverse events or undesirable side effects, the FDA, the IRBs at the institutions in which our studies are conducted, or a DSMB, could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

While the active pharmaceutical ingredient in SPR994, tebipenem, is approved in Japan, our formulation of tebipenem, SPR994, has not yet been tested in patients. There may be unforeseen serious adverse events or side effects that differ from those seen in the Japanese studies. To date, patients treated with the active ingredient in SPR994 have experienced drug-related side effects including diarrhea, temporary increases in hepatic enzymes, allergic reactions, rash, and convulsions. To date, SPR994 has generally been well tolerated in clinical trials conducted in healthy subjects and there have been no reports of serious adverse events related to SPR994, but additional adverse events may emerge in any subsequent clinical trials.

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

Undesirable side effects or other unexpected adverse events or properties of SPR994 or any of our other product candidates could arise or become known either during clinical development or, if approved, after the approved product has been marketed. If such an event occurs during development, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of, or could deny approval of, SPR994 or our other product candidates. If such an event occurs after such product candidates are approved, a number of potentially significant negative consequences may result, including:

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

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

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

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

In addition, we may face competition in enrolling suitable patients in any such trial as a result of other companies conducting clinical trials for antibiotic product candidates that are intended to treat similar infections, resulting in slower than anticipated

enrollment in our trials. Enrollment delays in any such trial may result in increased development costs for SPR741, or slow down or halt our product development and approval process for SPR741.

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

Even if we obtain FDA or other regulatory approvals and are able to launch SPR994 or any other product candidate commercially, the product candidate may not achieve market acceptance among physicians, patients, hospitals (including pharmacy directors) and third-party payors and, ultimately, may not be commercially successful. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of coverage and reimbursement for existing therapies. Market acceptance of any product candidate for which we receive approval depends on a number of factors, including:

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

Any failure by SPR994 or any other product candidate that obtains regulatory approval to achieve market acceptance or commercial success would adversely affect our business prospects.

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

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

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other

royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing SPR994 or any other product candidate if such product candidate is approved.

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

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

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

We intend to use collaborators to assist with the commercialization of SPR994 and any other product candidate outside the United States. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us would likely be lower than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we likely would have little control over such third parties, and any of them might fail to devote the necessary resources and attention to sell and market our products effectively.

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

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

The development and commercialization of new drug products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to SPR994 and our other product candidates that we may seek to develop and commercialize in the future. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of resistant infections. Potential competitors also include academic institutions, government agencies and other public and private research organizations. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than SPR994 or any other product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete and noncompetitive.

There are a variety of available oral therapies marketed for the treatment urinary tract infections that we would expect would compete with SPR994, such as Levaquin, Cipro and Bactrim. Many of the available therapies are well established and widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products, for example in the fluoroquinolone class. However, the susceptibility of urinary tract pathogens to the existing treatment alternatives is waning. If SPR994 is approved, the pricing may be at a significant premium over other competitive products. This may make it difficult for SPR994 to compete with these products.

There are also a number of oral product candidates in clinical development by third parties that are intended to treat UTIs. Some mid- to late-stage product candidates include ceftibuten/clavulanate (“C-Scape”) from Achaogen, Inc., sulopenem from Iterum Therapeutics Limited, and omadacycline from Paratek Pharmaceuticals, Inc. If our competitors obtain marketing approval from the

FDA or comparable foreign regulatory authorities for their product candidates more rapidly than us, it could result in our competitors establishing a strong market position before we are able to enter the market.

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

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

In July 2012, the Food and Drug Administration Safety and Innovation Act was passed, which included the Generating Antibiotics Incentives Now Act, or the GAIN Act. The GAIN Act is intended to provide incentives for the development of new, qualified infectious disease products. In December 2016, the Cures Act was passed, providing additional support for the development of new infectious disease products. These incentives may result in more competition in the market for new antibiotics, and may cause pharmaceutical and biotechnology companies with more resources than we have to shift their efforts towards the development of product candidates that could be competitive with SPR994 and our other product candidates.

Even if we are able to commercialize SPR994 or any other product candidate, the product may become subject to unfavorable pricing regulations, or third-party payor coverage and reimbursement policies that could harm our business.

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

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

To the extent SPR994 or any other product candidate we develop is used in an outpatient setting, the commercial success of our product candidates will depend substantially, both domestically and abroad, on the extent to which coverage and reimbursement for these products and related treatments are available from government health programs and third-party payors. If coverage is not available, or reimbursement is limited, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investments. Government authorities and third-party payors, such as health insurers and managed care organizations, publish formularies that identify the medications they will cover and the related payment levels. The healthcare industry is focused on cost containment, both in the United States and elsewhere. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell our product candidates profitably.

Increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We cannot be sure that coverage will be available for SPR994 or any other product candidate that we commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for outpatient drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any approved products used on an outpatient basis that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

We cannot predict whether bacteria may develop resistance to SPR994 or our other product candidates, which could affect their revenue potential.

We are developing SPR994 and certain of our other product candidates to treat drug-resistant bacterial infections. The bacteria responsible for these infections evolve quickly and readily transfer their resistance mechanisms within and between species. We cannot predict whether or when bacterial resistance to SPR994 or any of such other product candidates may develop.

As a carbapenem, SPR994 is not active against organisms expressing a resistance mechanism mediated by enzymes known as carbapenemases. Although occurrence of this resistance mechanism is currently rare, we cannot predict whether carbapenemase-mediated resistance will become widespread in regions where we intend to market SPR994 if it is approved. The growth of drug resistant infections in community settings or in countries with poor public health infrastructures, or the potential use of SPR994 or any of our other product candidates outside of controlled hospital settings, could contribute to the rise of resistance. If resistance to SPR994 or any of our other product candidates becomes prevalent, our ability to generate revenue from SPR994 or such product candidates could suffer.

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

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

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

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

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

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

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we obtain marketing approval for and commercially sell SPR994 or any other product candidate. For example, we may be sued if any product that we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

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

Although we maintain general liability insurance and clinical trial liability insurance, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if and when we receive marketing approval for and begin selling SPR994 or any other product candidate. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could adversely affect our business, financial condition, results of operations and prospects.

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

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

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

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

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

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

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

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

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

Risks Related to Our Dependence on Third Parties

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

Although we expect to commercialize SPR994 ourselves in the United States, we intend to commercialize it outside the United States through collaboration arrangements. If we develop SPR741 to be co-administered in combination with branded and not generic antibiotic compounds, then we will be required to obtain and maintain rights from third-party collaborators for the development and commercialization of SPR741 co-administered with such other branded antibiotic compounds. In addition, we may seek third-party collaborators for development and commercialization of certain of our product candidates. For instance, in January 2019, we entered into a license agreement with Everest Medicines II Limited whereby we granted Everest an exclusive license to develop, manufacture and commercialize SPR206, or products containing SPR206, in Greater China, South Korea and certain Southeast Asian countries. In addition to the license grant with respect to SPR206, we also granted to Everest a 12-month exclusive option to negotiate with us for an exclusive license to develop, manufacture or commercialize SPR741 in the same territories. Our likely collaborators for any other marketing, distribution, development, licensing or broader collaboration arrangements we may pursue include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

We may derive revenue from research and development fees, license fees, milestone payments and royalties under any collaborative arrangement into which we enter. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, our collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations,

prior to or upon the expiration of the agreed upon terms. As a result, we can expect to relinquish some or all of the control over the future success of a product candidate that we license to a third party.

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

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

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

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

We will require additional funds to complete the development and potential commercialization of SPR994 and our other product candidates. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. Moreover, we intend to utilize a variety of types of collaboration arrangements for the potential commercialization of our product candidates outside the United States. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include:

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

- the need to seek licenses or sub-licenses to third-party intellectual property; and
- industry and market conditions generally.

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

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

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

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

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

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time and resources to our ongoing development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates. If that occurs, we may not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In such an event, our financial results and the commercial prospects for SPR994 or our other product candidates could be harmed, our costs could increase and our ability to generate revenue could be delayed, impaired or foreclosed.

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

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

We do not currently have nor do we plan to build the internal infrastructure or capability to manufacture SPR994 or our other product candidates for use in the conduct of our preclinical research, our clinical trials or for commercial supply. We currently rely on and expect to continue to rely on third-party contract manufacturers to manufacture supplies of SPR994 and our other product candidates, and we expect to rely on third-party contract manufacturers to manufacture commercial quantities of any product candidate that we commercialize following approval for marketing by applicable regulatory authorities, if any. Reliance on third-party manufacturers entails risks, including:

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

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

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

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

Our current and anticipated future dependence upon others for the manufacture of SPR994 and our other product candidates and potential product candidates may adversely affect our future profit margins and our ability to commercialize any products for which we receive marketing approval on a timely and competitive basis.

If we fail to comply with our obligations in the agreements under which we in-license or acquire development or commercialization rights to products, technology or data from third parties, including those for SPR994, we could lose such rights that are important to our business.

We are a party to agreements with Meiji for SPR994, Northern for SPR741, Vertex Pharmaceuticals for SPR720 and PBB Distributions Limited for SPR206, and we may enter into additional agreements, including license agreements, with other parties in the future that impose diligence, development and commercialization timelines, milestone payments, royalties, insurance and other obligations on us.

For example, we have an exclusive know-how license with Meiji, or the Meiji License, that gives Spero rights outside of specified countries in Asia to develop, manufacture, and commercialize SPR994 as well as the right to use, cross-reference, file or incorporate by reference any information and relevant Meiji regulatory documentation to support any regulatory filings outside of Asia. In addition, Spero has the right to develop, manufacture and have manufactured SPR994 in Asia solely for the purpose of furthering development, manufacturing and commercialization of SPR994 outside of Asia. In exchange for those rights, Spero is obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop and commercialize SPR994 and to implement a specified development plan, meeting specified development milestones and providing an update on progress on an annual basis. The Meiji License requires us to pay milestone payments of up to $3.0 million upon the achievement of specified clinical and regulatory milestones and royalties of a low single-digit percentage on net sales on a country-by-country basis.

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

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

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

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

- terminate agreements, in whole or in part, for any reason or no reason;
- reduce or modify the government's obligations under such agreements without the consent of the contractor;
- claim rights, including intellectual property rights, in products and data developed under such agreements;
- audit contract-related costs and fees, including allocated indirect costs;
- suspend the contractor from receiving new contracts pending resolution of alleged violations of procurement laws or regulations;
- impose U.S. manufacturing requirements for products that embody inventions conceived or first reduced to practice under such agreements;
- suspend or debar the contractor or grantee from doing future business with the government;
- control and potentially prohibit the export of products; and
- pursue criminal or civil remedies under the False Claims Act, or the FCA, the False Statements Act and similar remedy provisions specific to government agreements.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Our Intellectual Property

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

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

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

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

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

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

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

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

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

In any infringement litigation, any award of monetary damages we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of

our confidential information could be compromised by disclosure during litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

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

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

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our technology or product candidates, including interference proceedings before the U.S. Patent and Trademark Office. Intellectual property disputes arise in a number of areas including with respect to patents, use of other proprietary rights and the contractual terms of license arrangements. Third parties may assert claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. With respect to our Meiji License of certain know-how used in SPR994, we are neither a party to, nor an express third-party beneficiary of, the letter agreement between Meiji and Global Pharma consenting to Meiji's arrangement with us. As such, if any dispute among the parties were to occur, our direct enforcement rights with respect to the letter agreement may be limited or uncertain. A termination or early expiration of the head license between Meiji and Global Pharma (which currently by its terms is set to expire in January 2022) or any restriction on our ability to use the Global Pharma know-how could have a negative impact on our development of SPR994 and adversely affect our business.

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

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

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

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

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

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

We have not yet registered our trademarks. Failure to secure those registrations could adversely affect our business.

We have not yet registered our trademarks in the United States or other countries. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would, which could adversely affect our business. We have also not yet registered trademarks for any of our product candidates in any jurisdiction. When we file trademark applications for our product candidates those applications may not be allowed for registration, and registered trademarks may not be obtained, maintained or enforced. During trademark registration proceedings in the United States and foreign jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but we may not be able to overcome such rejections. In addition, in the United States Patent and Trademark Office and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings.

In addition, any proprietary name we propose to use with SPR994 or any other product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize SPR994 or our other product candidates, and our ability to generate revenue will be materially impaired.

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

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

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

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

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

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

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

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

If a drug is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a drug sponsor may apply for fast track designation by the FDA for the particular indication

under study. If fast track designation is obtained, the FDA may initiate review of sections of an NDA before the application is complete. This "rolling review" is available if the applicant provides and the FDA approves a schedule for the remaining information. If we seek fast track designation for a product candidate, we may not receive it from the FDA. However, even if we receive fast track designation, fast track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with fast track designation compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

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

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

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

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

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

In order to market and sell SPR994 or our other product candidates in the European Union and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The approval procedure varies among countries and can involve additional testing. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis or at all.

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

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

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

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

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

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

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

- the federal healthcare Anti-Kickback Statute, among other things, prohibits persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federally funded healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate the statute in order to have committed a violation. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

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

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

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

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

policy changes from payors may reduce payments for any products for which we obtain marketing approval and could affect future revenues.

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

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

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

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. There have been several U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the effect of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

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

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

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

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

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

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

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

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

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

Risks Related to Employee Matters and Managing Growth

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

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Ankit Mahadevia, M.D., our President and Chief Executive Officer, as well as the other principal members of our management, scientific and clinical team. Although we have formal

employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time.

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

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

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

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

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

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

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

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

In the future, we may enter into transactions to acquire other businesses, products or technologies. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company,

which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Risks Related to Our Common Stock

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

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

- the success of existing or new competitive products or technologies;
- the timing of clinical trials of SPR994 and any other product candidate;
- results of clinical trials of SPR994 and any other product candidate;
- failure or discontinuation of any of our development programs;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- the perception of the pharmaceutical and biotechnology industry by the public, legislatures, regulators and the investment community;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to develop, in-license or acquire additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

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

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

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

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

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

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

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

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

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

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

We are an "emerging growth company," as defined in the JOBS Act, and may remain an emerging growth company for up to five years. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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

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

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

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

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

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

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

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

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

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

As of March 31, 2019, our executive officers and directors, combined with our stockholders who as of such date owned more than 5% of our outstanding common stock, in the aggregate, beneficially own shares representing approximately 56% of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

- delay, defer or prevent a change in control;

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

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated by-laws may discourage, delay or prevent a merger, acquisition or other change in control of us that our stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that all members of the board are not elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call a special meeting of stockholders;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast to amend or repeal certain provisions of our certificate of incorporation or by-laws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

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

As of March 31, 2019, we had used approximately $71.2 million from the net proceeds from our IPO.

Item 6. Exhibits

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
31.1	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X			
31.2	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X			
32.1	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X			
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X			
101.INS	XBRL Instance Document	X			
101.SCH	XBRL Taxonomy Extension Schema Document	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	XBRL Taxonomy Extension Definition	X			
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	XBRL Taxonomy Presentation Linkbase Document	X			

SIGNATURES

Pursuant to the requirements 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: May 9, 2019

By: /s/ Ankit Mahadevia, M.D.
Ankit Mahadevia, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: May 9, 2019

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

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Ankit Mahadevia, M.D., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Spero Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal controls over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

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

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

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

Date: May 9, 2019

By: /s/ Ankit Mahadevia, M.D.
Ankit Mahadevia, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Joel Sendek, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Spero Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal controls over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

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

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

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

Date: May 9, 2019

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

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Spero Therapeutics, Inc. (the "Company") for the period ended March 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: May 9, 2019

By: /s/ Ankit Mahadevia, M.D.
Ankit Mahadevia, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Spero Therapeutics, Inc. (the "Company") for the period ended March 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: May 9, 2019

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