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, 2022

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)

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

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 ☒

As of May 12, 2022, the registrant had 32,821,544 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;
- the timing and outcome of the New Drug Application (“NDA”) approval process for tebipenem HBr and the potential for a partnership of the tebipenem HBr franchise;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the timing or likelihood of regulatory filings and approvals;
- the direct and indirect impact of the pandemic caused by an outbreak of a new strain of coronavirus (“COVID-19”) on our business and operations, including manufacturing, research and development costs, clinical trials, regulatory processes and employee expenses;
- the future development and commercialization of our product candidates, if approved;
- the pricing, coverage and reimbursement of our product candidates, if approved;
- the implementation of our business model and strategic plans for our business and product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates;
- our ability to enter into strategic arrangements and/or collaborations and the potential benefits of such arrangements;
- the expected cost-savings from our announced strategic restructuring;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- our ability to continue as a going concern;
- our financial performance;
- developments relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under Part 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.

Risk Factor Summary

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

- Pursuant to our recently announced restructuring, we have suspended all commercialization efforts with respect to tebipenem HBr and have shifted our focus and resources to advancing the clinical development of our other programs, SPR720 and SPR206, while continuing our dialogue with the FDA to seek a pathway forward for the potential approval of tebipenem HBr. If we fail to execute successfully on this re-prioritized strategic focus, our business and prospects may be adversely affected.
- Based on our recent feedback from the FDA, the timing and terms of any potential approval of tebipenem HBr remain uncertain, which may impact our ability to realize the value of tebipenem HBr.
- If the evidence submitted with our NDA for our product candidates fail to demonstrate safety and efficacy to the satisfaction of the United States Food and Drug Administration ("FDA") or comparable foreign regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.
- Our analyses based on preliminary or interim data from our clinical studies that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- Serious adverse events or undesirable side effects or other unexpected properties of any of our product candidates may be identified during development or after approval that could delay, prevent or cause the withdrawal of regulatory approval, limit the commercial potential, or result in significant negative consequences following marketing approval.
- Even if a product candidate does obtain regulatory approval, it may never achieve the market acceptance by physicians, patients, hospitals, third-party payors and others in the medical community that is necessary for commercial success and the market opportunity may be smaller than we estimate.
- If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing any of our product candidates if such product candidate is approved.
- We face substantial competition from other pharmaceutical and biotechnology companies and our operating results may suffer if we fail to compete effectively.
- Our Revenue Interest Financing Agreement ("Revenue Interest Agreement") with HealthCare Royalty Management, LLC ("HCR") could limit cash flow available for our operations and expose us to risks that could adversely affect our business, financial condition and results of operations.
- We have not generated any revenue from the sale of our products, have a history of losses and expect to incur substantial future losses. The report of our auditor on our consolidated financial statements expresses substantial doubt about our ability to continue as a going concern; if we are unable to obtain additional capital, we may not be able to continue our operations on the scope or scale as currently conducted, and that could have a material adverse effect on our business, results of operations and financial condition.
- We expect that we will need substantial additional funding. If we are unable to raise capital when needed, or do not receive payment under our government awards, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- The continued COVID-19 pandemic could adversely impact our business, including our preclinical studies and clinical trials.
- We expect to depend on collaborations with third parties for the development and commercialization of some of our product candidates. Our prospects with respect to those product candidates will depend in part on the success of those collaborations.
- We contract with third parties for the manufacture of preclinical and clinical supplies of our product candidates and expect to continue to do so in connection with any future commercialization and for any future clinical trials and commercialization of our other product candidates and potential product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

- Our use of government funding for certain of our programs adds complexity to our research and commercialization efforts with respect to those programs and may impose requirements that increase the costs of commercialization and production of product candidates developed under those government-funded programs.
- If we are unable to obtain and maintain sufficient patent protection for our technology or our product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and product candidates may be adversely affected.
- We have registered trademarks and pending trademark applications. Failure to enforce our registered marks or secure registration of our pending trademark applications could adversely affect our business.
- If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.
- We are undertaking internal restructuring activities that could result in disruptions to our business or otherwise materially harm our results of operations or financial condition.

Spero Therapeutics, Inc.
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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, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 72,111	$ 112,584
Marketable securities	49,855	33,818
Other receivables	1,620	2,280
Tax incentive receivable, current	371	361
Prepaid expenses and other current assets	8,747	8,829
Total current assets	132,704	157,872
Property and equipment, net	888	1,026
Operating lease right of use assets	6,309	6,530
Other assets	5,929	5,644
Total assets	$ 145,830	$ 171,072
Liabilities and Stockholders' Equity		
Current liabilities:		
Liability related to the sale of future royalties, current	$ 50,902	$ —
Accounts payable	4,780	1,101
Accrued expenses and other current liabilities	9,060	14,350
Operating lease liabilities	1,369	1,362
Deferred revenue, current	2,093	1,857
Derivative liability, current	995	-
Total current liabilities	69,199	18,670
Liability related to the sale of future royalties, non-current	—	48,414
Non-current operating lease liabilities	5,726	5,973
Deferred revenue, non-current	8,304	8,786
Derivative liability, non-current	—	802
Other long-term liabilities	128	138
Total liabilities	83,357	82,783
Commitments and contingencies (Note 7)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized, 3,218,152 shares issued and outstanding as of March 31, 2022 and 3,218,152 shares issued and outstanding as of December 31, 2021	3	3
Common stock, $0.001 par value; 120,000,000 shares authorized as of March 31, 2022 and December 31, 2021; 32,755,559 shares issued and outstanding as of March 31, 2022 and 32,393,738 shares issued and outstanding as of December 31, 2021	33	32
Additional paid-in capital	462,735	455,719
Accumulated deficit	(400,292)	(367,463)
Accumulated other comprehensive gain (loss)	(6)	(2)
Total stockholders' equity	62,473	88,289
Total liabilities and stockholders' equity	$ 145,830	$ 171,072

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,	
	2022	2021
Revenues:		
Grant revenue	$ 1,822	$ 7,300
Collaboration revenue	247	—
Total revenues	2,069	7,300
Operating expenses:		
Research and development	16,971	18,404
General and administrative	15,305	8,299
Total operating expenses	32,276	26,703
Loss from operations	(30,207)	(19,403)
Other income (expense):		
Interest income	72	98
Other income (expense), net	(13)	(118)
Interest expense related to the sale of future royalties	(2,488)	—
Change in fair value of derivative liability	(193)	—
Total other income (expense), net	(2,622)	(20)
Net loss	$ (32,829)	$ (19,423)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.01)	$ (0.66)
Weighted average common shares outstanding, basic and diluted:	32,606,715	29,414,148
Comprehensive loss:		
Net loss	(32,829)	(19,423)
Other comprehensive gain (loss):		
Unrealized gain (loss) on marketable securities	(4)	4
Net unrealized gains (losses) on securities	(4)	4
Total comprehensive loss	$ (32,833)	$ (19,419)

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,	
	2022	**2021**
Cash flows from operating activities:		
Net loss	$ (32,829)	$ (19,423)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	189	159
Non-cash lease cost	221	199
Share-based compensation	3,203	2,009
Unrealized foreign currency transaction (gain) loss	(11)	(19)
Accretion of discount on marketable securities	23	64
Change in fair value of derivative liabilities	193	—
Non-cash interest expense associated with the sale of future royalties	2,488	—
Changes in operating assets and liabilities:		
Other receivables	660	(3,218)
Prepaid expenses and other current assets	31	869
Tax incentive receivables	1	772
Other assets	(285)	—
Accounts payable	3,679	2,689
Accrued expenses and other current liabilities	(5,290)	624
Deferred revenue, current and non-current	(246)	—
Other long-term liabilities	(10)	(9)
Operating lease liability	(240)	(195)
Net cash used in operating activities	(28,223)	(15,479)
Cash flows from investing activities:		
Purchases of marketable securities	(26,970)	(2,997)
Proceeds from maturities of marketable securities	10,906	6,000
Net cash provided by (used in) investing activities	(16,064)	3,003
Cash flows from financing activities:		
Proceeds from the issuance of common stock, net of issuance costs	3,626	4,253
Payment of offering and financing costs	—	(37)
Proceeds from stock option exercises	188	93
Net cash provided by financing activities	3,814	4,309
Net increase (decrease) in cash and cash equivalents	(40,473)	(8,167)
Cash, cash equivalents and restricted cash at beginning of period	112,584	85,209
Cash, cash equivalents and restricted cash at end of period	$ 72,111	$ 77,042
Supplemental disclosure of non-cash activities:		
Offering and financing costs in accounts payable and accruals	$ —	$ 93

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)
(Unaudited)

	Series A, B, C and D Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Spero Therapeutics, Inc. Stockholders' Equity
	Shares	Par Value	Shares	Par Value				
Balances at December 31, 2021	**3,218,152**	**3**	**32,393,738**	**32**	**455,719**	**(367,463)**	**(2)**	**88,289**
Issuance of common stock upon the exercise of stock options	—	—	17,616	—	188	—	—	188
Issuance of common stock, net of issuance costs	—	—	344,205	1	3,625	—	—	3,626
Share-based compensation expense	—	—	—	—	3,203	—	—	3,203
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	(4)	(4)
Net loss	—	—	—	—	—	(32,829)	—	(32,829)
Balances at March 31, 2022	**3,218,152**	**3**	**32,755,559**	**33**	**462,735**	**(400,292)**	**(6)**	**62,473**

	Series A, B, C and D Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Spero Therapeutics, Inc. Stockholders' Equity
	Shares	Par Value	Shares	Par Value				
Balances at December 31, 2020	**3,218,287**	**3**	**29,260,247**	**29**	**409,722**	**(277,707)**	**(7)**	**132,040**
Issuance of common stock upon the exercise of stock options	—	—	11,514	—	93	—	—	93
Issuance of common stock, net of financing costs of $130 and net of issuance costs	—	—	257,185	1	4,122	—	—	4,123
Conversion of convertible preferred stock to common stock	(135)	—	135,000	—	—	—	—	—
Share-based compensation expense	—	—	—	—	2,009	—	—	2,009
Unrealized gain on available-for-sale securities	—	—	—	—	—	—	4	4
Net loss	—	—	—	—	—	(19,423)	—	(19,423)
Balances at March 31, 2021	**3,218,152**	**3**	**29,663,946**	**30**	**415,946**	**(297,130)**	**(3)**	**118,846**

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

1. Nature of the Business and Basis of Presentation

Spero Therapeutics, Inc., together with its consolidated subsidiaries (the "Company" or "Spero"), is a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing, and commercializing novel treatments for bacterial infections, including multi-drug resistant ("MDR") bacterial infections, and rare diseases. The Company's most advanced product candidate, tebipenem pivoxil hydrobromide or tebipenem HBr (previously SPR994), is designed to be the first broad-spectrum oral carbapenem-class antibiotic for use to treat certain bacterial infections that cause complicated urinary tract infections ("cUTIs"), including pyelonephritis, caused by certain microorganisms, in adult patients who have limited oral treatment options. Treatment with effective orally administrable antibiotics may prevent hospitalizations for serious infections and enable earlier and cost-effective treatment of patients after hospitalization. The Company is also developing SPR720, a novel oral antibiotic designed for the treatment of a rare, orphan disease caused by non-tuberculous mycobacterial pulmonary infections ("NTM"). In addition, the Company is developing an IV-administered product candidate, SPR206, to treat MDR Gram-negative infections in the hospital.

The Company is subject to risks and uncertainties common to companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations, risks of failure or unsatisfactory results of nonclinical studies and clinical trials, the need to obtain marketing approval for its product candidates, the need to successfully commercialize and gain market acceptance of its product candidates and the ability to secure additional capital to fund operations. The Company's product candidates will require additional preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales. The pandemic caused by COVID-19 has resulted, and is likely to continue to result, in significant national and global economic disruption and may adversely affect our business. The Company has experienced impacts to its clinical and development timelines due to the worldwide spread of COVID-19 and its variants. However, to date, the Company has not experienced material impacts to liquidity, nor has it incurred impairment of any assets as a result of COVID-19 or its variants. The Company continues to monitor this situation and the possible effects on its business, results of operations and financial condition, including manufacturing, clinical trials, research and development costs and employee-related amounts.

On May 3, 2022, the Company announced that it would immediately suspend current commercialization activities for tebipenem HBr based on feedback from a recent Late Cycle Meeting ("LCM") with the FDA regarding its NDA for tebipenem HBr. Although the review is still ongoing and the FDA has not yet made any final determination regarding approvability, the discussion suggested that the data package may be insufficient to support approval during this review cycle. In connection with this development, the Company announced that it is undertaking a reduction in its workforce by approximately 75% and a restructuring of its operations to reduce operating costs and reallocate resources towards the clinical development programs of SPR720 and SPR206, while continuing engagement with the FDA on the appropriate path forward for tebipenem HBr. Refer to Note 13 "Subsequent Events" for further information.

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

Since inception, the Company has funded its operations with proceeds from sales of preferred units (including bridge units, which converted into preferred units), payments received in connection with its collaboration agreements, funding from government contracts, licensing agreements and through the sale of the Company's common and preferred stock. The Company has incurred recurring losses since inception, including net losses of $32.8 million and $19.4 million for the three months ended March 31, 2022 and 2021, respectively. In addition, as of March 31, 2022, the Company had an accumulated deficit of $400.3 million. The Company expects to continue to generate operating losses for the foreseeable future.

In accordance with Accounting Standards Update ("ASU") 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40), the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that these consolidated financial statements are issued. Based on the Company's current operating plan and existing cash, cash equivalents and marketable securities, the Company has determined that there is substantial doubt regarding its ability to continue as a going concern within one year after the date that these consolidated financial statements are issued due to uncertainty in future projections and the timing and outcome of the approval process for tebipenem HBr. The Company will require additional funding to

fund the development of its product candidates through regulatory approval and commercialization, and to support its continued operations. The Company will seek additional funding through public or private financings, debt financing, collaboration agreements, government grants or other venues. The COVID-19 pandemic has resulted in ongoing volatility in financial markets. If our access to capital is restricted or associated borrowing costs increase as a result of developments in financial markets, including relating to the COVID-19 pandemic or its variants, our operations and financial condition could be adversely impacted. There is no assurance that the Company will be successful in obtaining sufficient funding on acceptable terms, if at all, and it could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could materially adversely affect its business prospects or its ability to continue operations.

The accompanying consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty. Accordingly, the consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern and which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

Interim Financial Information

The consolidated balance sheet at December 31, 2021 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, 2022, and for the three months ended March 31, 2022, 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, 2021, included in the Company's Annual Report on Form 10-K for the year ended December 31, 2021, on file with the 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, 2022, and results of operations for the three months ended March 31, 2022, and cash flows for the three months ended March 31, 2022 and 2021 have been made. The results of operations for the three months ended March 31, 2022 are not necessarily indicative of the results of operations that may be expected for the year ending December 31, 2022.

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

Segment Information

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's singular focus is on identifying, developing and commercializing novel treatments for bacterial infections, including MDR bacterial infections, and rare diseases. All of the Company's tangible assets are held in the United States.

Concentrations of Credit Risk and of Significant Suppliers

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

The Company is dependent on third-party manufacturers to supply products for research and development activities in its programs. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs. As of March 31, 2022, and December 31, 2021, the Company had no off-balance sheet risk such as foreign exchange contracts, option contracts, or other hedging arrangements.

Cash Equivalents

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

Marketable Securities

Marketable securities consist of investments in corporate obligations with original maturities greater than 90 days. The Company considers its portfolio of investments to be available-for-sale. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Investments with maturities beyond one year are generally classified as short term, based on their highly liquid nature and because such marketable securities represent the investment of cash that is available for current operations. Unrealized gains and losses are reported as a component of accumulated other comprehensive income (loss) in stockholders' equity. Realized gains and losses and declines in value are included as a component of other income (expense), net based on the specific identification method. Any credit impairments are recorded through an allowance account.

Property and Equipment

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

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

Costs for capital assets not yet placed into service are capitalized as construction in progress and are depreciated in accordance with the above guidelines once placed into service. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance are charged to expense as incurred. The Company periodically evaluates whether events and circumstances have occurred that may warrant revision of the estimated useful life of property and equipment.

Leases

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company has elected not to recognize on the balance sheet leases with terms of one year or less. As of March 31, 2022, the Company had no short-term leases with terms of one year or less. Options to renew a lease are not included in the Company's initial lease term assessment unless there is reasonable certainty that the Company will renew. The Company monitors its plans to renew its material leases on a quarterly basis.

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

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

Other Assets

Other assets consist of long-term prepayments and deposits.

Impairment of Long-Lived Assets

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

Fair Value Measurements

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

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

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

Revenue Recognition – Collaboration Revenue

Effective June 30, 2021, 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 arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in the arrangements. 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.

Government Tax Incentives

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

Since the fourth quarter of 2016, the Company's operating subsidiary in Australia has met the eligibility requirements to receive a tax incentive for qualifying research and development activities (see Note 11). The Company recognizes these incentives as a reduction of research and development expenses in the consolidated statements of operations and comprehensive loss in the same period that the related qualifying expenses are incurred. Reductions of research and development expense recognized upon incurring qualifying expenses in advance of receipt of tax incentive payments are recorded in the consolidated balance sheet as tax incentive receivables.

Research and Development Costs

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

Clinical Trial and other Research Contract Costs and Accruals

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

Patent Costs

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

Share-Based Compensation

The Company issues stock-based awards to employees and directors in the form of stock options and restricted stock units. The Company measures and recognizes compensation expense for its stock-based awards granted to its employees and directors based on the estimated grant date fair value in accordance with ASC 718, Compensation—Stock Compensation, and determines the fair value of restricted stock units based on the fair value of its common stock. The Company measures all share-based options granted to employees and directors based on the fair value on the date of grant using the Black-Scholes option-pricing model. Compensation expense of those awards is recognized over the requisite service period, which is generally the vesting period of the respective award. The Company records the expense for awards with service-based conditions using the straight-line method over the requisite service period, net of any actual forfeitures. The Company has also granted certain awards subject to performance-based vesting eligibility and a subsequent partial time-based vesting schedule. The Company classifies share-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with shareholders. For the three months ended March 31, 2022 and 2021, these changes related to unrealized gains and losses on the Company's available-for-sale marketable securities.

Net Loss per Share

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

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

Income Taxes

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

In addition, the CARES Act raises the corporate charitable deduction limit to 25% of taxable income and makes qualified improvement property generally eligible for 15-year cost-recovery and 100% bonus depreciation. The enactment of the CARES Act did not result in any material adjustments to our income tax provision for the three months ended March 31, 2022, or to our net deferred tax assets as of March 31, 2022.

Liability related to the sale of future royalties

The Company treats the liability related to the sale of future royalties, as discussed further in Note 10, as a debt instrument, amortized under the effective interest rate method over the estimated life of the revenue streams. The Company recognizes interest expense thereon using the effective rate, which is based on its current estimates of future revenues over the life of the arrangement. The Company periodically assesses its expected revenues using internal projections, imputes interest on the carrying value of the deferred royalty obligation and records interest expense using the imputed effective interest rate. To the extent its estimates of future revenues are greater or less than previous estimates or the estimated timing of such payments is materially different than previous estimates, the Company will account for any such changes by adjusting the effective interest rate on a prospective basis, with a corresponding impact to the reclassification of the deferred royalty obligation. The assumptions used in determining the expected repayment term of the deferred royalty obligation and amortization period of the issuance costs requires that the Company makes estimates that could impact the short-term and long-term classification of such costs, as well as the period over which such costs will be amortized.

Derivative Liability

In connection with certain transactions, the Company has identified certain embedded derivatives, which are recorded as liabilities on the Company's consolidated balance sheet and are remeasured to fair value at each reporting date until the derivative is settled. Changes in the fair value of the derivative liabilities are recognized as other income (expense) in the consolidated statement of operations and comprehensive loss.

Recently Issued and Adopted Accounting Pronouncements

Other accounting standards that have been issued by the Financial Accounting Standards Board or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on our financial statements upon adoption.

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, 2022 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ —	$ 37,803	$ —	$ 37,803
Corporate bonds	—	2,718	—	2,718
U.S. government securities	—	5,998	—	5,998
Total cash equivalents	—	46,519	—	46,519
Marketable securities:				
Corporate bonds		7,928		7,928
Commercial paper	—	14,944	—	14,944
U.S. government securities	—	26,983	—	26,983
Total marketable securities	—	49,855	—	49,855
Total cash equivalents and marketable securities	—	96,374	—	96,374
Liabilities:				
Derivative liability	$ —	$ —	$ 995	$ 995
	$ —	$ —	$ 995	$ 995

	Fair Value Measurements at December 31, 2021 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ —	$ 109,316	$ —	$ 109,316
Corporate bonds	—	2,701	—	2,701
Total cash equivalents	—	112,017	—	112,017
Marketable securities:				
Corporate bonds	—	11,479	—	11,479
Commercial paper	—	22,339	—	22,339
Total marketable securities	—	33,818	—	33,818
Total cash equivalents and marketable securities	$ —	$ 145,835	$ —	$ 145,835
Liabilities:				
Derivative liability	$ —	$ —	$ 802	$ 802
	$ —	$ —	$ 802	$ 802

Excluded from the tables above is cash of $25.6 million and $0.6 million as of March 31, 2022, and December 31, 2021, respectively. During the three months ended March 31, 2022, there were no transfers between Level 1, Level 2 and Level 3 categories.

Marketable Securities

The Company's marketable securities are classified as Level 2 assets under the fair value hierarchy as these assets were primarily determined from independent pricing sources, which generally derive security prices from recently reported trades for identical or similar securities. The Company evaluated debt securities with unrealized losses for any expected credit losses and determined unrealized losses on these securities were related to non-credit factors. Additionally, the Company currently does not intend to and is not required to sell these investments prior to an anticipated recovery in value.

The following table summarizes the gross unrealized gains and losses of the Company's marketable securities as of March 31, 2022, and December 31, 2021 (in thousands):

	March 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets:				
Corporate bonds	$ 7,934	$ —	$ (6)	$ 7,928
Commercial paper	14,944	—	—	14,944
U.S. government securities	26,981	2	—	26,983
	$ 49,859	$ 2	$ (6)	$ 49,855

	December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets:				
Corporate bonds	$ 11,481	$ —	$ (2)	$ 11,479
Commercial paper	22,339	—	—	22,339
	$ 33,820	$ —	$ (2)	$ 33,818

As of March 31, 2022, and December 31, 2021, all of the Company's marketable securities had remaining contractual maturity dates of one year or less from the respective consolidated balance sheet date.

Embedded Derivative

In connection with the liability related to the sale of future royalties (see Note 10), the Company classified $1.0 million at inception of its Revenue Interest Agreement (as defined below) as a derivative liability on its consolidated balance sheet because there were embedded instruments that represent a conditional obligation to pay HCR the final payment, which is 250% of the Investment Amount (as defined below), upon an event of default or change of control. The Company will remeasure the derivative liability to fair value at each reporting date, and recognize 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 Company valued its change of control provision under the Revenue Interest Agreement using a Monte Carlo Simulation Method, assuming a lognormal distribution for revenue. The assumptions used in the valuation model include (1) our estimates of the probability and timing of related events, (2) our estimates of future revenues subject to the Revenue Interest Agreement, (3) volatility, (4) the risk-adjusted discount rate and (5) the probability of a change in control occurring during the term of the instrument.

The fair value of the derivative liability upon issuance in October 2021 was $1.0 million, and is classified as Level 3 liability under the fair value hierarchy.

The fair value of the derivative liability increased from $0.8 million as of December 31, 2021 to $1.0 million as of March 31, 2022, primarily due to the passage of time and changes in the market volatility and underlying credit risk inputs.

Liability related to the sale of future royalties

The fair value for the liability related to the sale of future royalties at the time of the transaction was based on the Company's current estimates of future royalties expected to be paid to HCR over the remaining patent life of the product, which are considered Level 3 inputs (see Note 10).

4. Accrued Expenses and Other Current Liabilities

The following table presents the Company's accrued expenses and other current liabilities as of March 31, 2022 and December 31, 2021 (in thousands):

	March 31, 2022	December 31, 2021
Accrued external research and development expenses	$ 4,147	$ 6,315
Accrued payroll and related expenses	2,397	5,884
Accrued professional fees	1,452	909
Accrued other	1,064	1,242
Total Accrued expenses and other current liabilities	$ 9,060	$ 14,350

5. Common Stock

On March 11, 2021, the Company entered into a new sales agreement with Cantor and filed a new universal shelf registration statement on Form S-3 (Registration No. 333-254170), and pursuant to which the Company registered for sale up to $300.0 million of any combination of its common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that the Company may determine, including up to $75.0 million of its common stock available for issuance pursuant to the new "at-the-market" offering program sales agreement that it entered into with Cantor. Under the new 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 new sales agreement. The Company's universal shelf registration statement on Form S-3 (Registration No. 333-254170) became effective on March 29, 2021 and its prior sales agreement with Cantor terminated automatically at such time.

In February 2021, a holder of the Company's Series B Preferred Stock elected to convert 62 shares of Series B Preferred Stock into 62,000 shares of the Company's common stock, pursuant to such holder's rights under the certificate of designation for such Series B Preferred Stock. In addition, a holder of the Company's Series C Preferred Stock elected to convert 73 shares of Series C Preferred Stock into 73,000 shares of the Company's common stock, pursuant to such holder's rights under the certificate of designation for such Series C Preferred Stock.

On June 30, 2021, the Company agreed to sell 2,362,348 shares of common stock to Pfizer Inc. ("Pfizer") pursuant to a Share Purchase Agreement (the "Pfizer Purchase Agreement"), at a price of $16.93 per share, which represented a premium over the most recent closing price on June 30, 2021, for an aggregate purchase price of $40.0 million. In addition, under the terms of the Pfizer Purchase Agreement, the shares are subject to a lock-up restriction, such that Pfizer will not, subject to certain limited exceptions, without the prior approval of the Company, sell or otherwise dispose of the shares until one year after the date of the closing of the sale of the shares under the Pfizer Purchase Agreement.

No shareholder approval was required for the sale of the shares. Pfizer is an accredited investor as defined in the Securities Act, and the shares were sold pursuant to exemptions from registration under Regulation D of the Securities Act. The Company has not filed a registration statement with the SEC covering the resale of the shares and such securities may not be offered or sold in the United States absent registration or an exemption from registration under the Securities Act and any applicable state securities laws.

The fair market value of 2,362,348 shares of the Company's common stock issued to Pfizer under the Pfizer Purchase Agreement was $27.5 million. The common stock issued under the Pfizer Purchase Agreement were valued using an option pricing valuation model as the shares are subject to certain holding period restrictions. The Company accounted for the associated premium of $12.5 million as a freestanding equity-linked instrument under ASC 815. The premium was allocated as consideration for the Company's license agreement with Pfizer (the "Pfizer License Agreement") and evaluated under ASC 606. The premium was determined not to be constrained and was included in the calculation of the total transaction price related to the Pfizer License Agreement as of June 30, 2021. Refer to Note 9 for further discussion.

The closing of the sale of the shares pursuant to the Pfizer Purchase Agreement occurred on July 1, 2021. Upon closing, the Company recorded the fair market value of the shares issued in stockholders' equity in its condensed consolidated balance sheet.

On August 17, 2021, the Company filed a Certificate of Amendment to its Amended and Restated Certificate of Incorporation with the Secretary of State of the State of Delaware to increase the number of shares of the Company's common stock authorized for

issuance from 60,000,000 shares to 120,000,000 shares (the "Charter Amendment"). The Charter Amendment was approved by the Company's stockholders at the Annual Meeting held on August 17, 2021.

During the three months ended March 31, 2022 the Company sold 344,205 shares of its common stock under its "at-the-market" offering sales agreement at an average price of approximately $10.86 per share for aggregate gross proceeds of approximately $3.7 million prior to deducting sales commissions.

6. Share-Based Compensation

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

In August 2021, the Company's shareholders approved amendments to the 2017 Plan. The amendments provide for the following: (i) increases the number of shares of the Company's common stock authorized for issuance under the 2017 Plan by 3,170,254 shares, (ii) removes the "evergreen" provision historically included in the 2017 Plan, and (iii) makes certain other amendments.

Stock Options

The weighted-average grant date fair value of options, estimated as of the grant date using the Black-Scholes option pricing model, was $7.96 and $14.57 per option for those options granted during the three months ended March 31, 2022 and 2021 respectively.

The following table summarizes stock option activity under all equity plans (excluding RSUs) during the three months ended March 31, 2022:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2021	4,890,716	$ 11.75	7.62	$ 24,263
Granted	952,604	11.15	—	—
Exercised	(17,616)	10.72	—	—
Forfeited or cancelled	(50,636)	14.80	—	
Outstanding as of March 31, 2022	5,775,068	$ 11.63	7.61	$ 3,951
Outstanding as of March 31, 2022 - vested and expected to vest	5,775,068	$ 11.63	7.61	$ 3,951
Exercisable at March 31, 2022	2,868,263	$ 9.47	6.29	$ 3,684

As of March 31, 2022, a total of 8,720,127 shares have been authorized and reserved for issuance under all equity plans and 1,143,299 shares were available for future issuance under such plans.

Restricted Stock Units

The Company granted 657,757 RSUs to employees during the three months ended March 31, 2022.

The following table summarizes RSU activity under all equity plans during the three months ended March 31, 2022:

	Number of RSU Shares	Weighted Average Grant Date Fair Value
Outstanding as of December 31, 2021	513,690	17.08
Granted	657,757	11.14
Vested and released	—	—
Forfeited or cancelled	(7,800)	15.51
Outstanding as of March 31, 2022	1,163,647	13.73

As of March 31, 2022, there was approximately $14.9 million of total unrecognized compensation expense related to RSUs, which is expected to be recognized over a weighted-average period of approximately 3.67 years.

The fair value of the RSUs is determined on the date of grant based on the market price of the Company's ordinary shares on that date. Each RSU represents the right to receive one share of the Company's common stock, $0.001 par value per share, upon vesting. The RSUs vest in four equal annual installments, subject to the individual's continued service to the Company through the applicable vesting date, and are subject to the terms and conditions of the Company's form of RSU agreement under the 2017 Plan.

Share-Based Compensation Expense

The Company recorded share-based compensation expense related to incentive stock options, nonqualified stock options, stock grants, and stock-based awards in the following expense categories of its consolidated statements of operations and comprehensive loss (in thousands):

	Three Months Ended March 31,	
	2022	2021
Research and development expenses	$ 1,363	$ 840
General and administrative expenses	1,840	1,169
Total	$ 3,203	$ 2,009

7. 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 9).

Operating Leases

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

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not aware of any claims under indemnification arrangements that will have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of March 31, 2022 or December 31, 2021.

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 any such legal proceedings.

8. Government Contracts

BARDA

In July 2018, the Company was awarded a contract from Biomedical Advanced Research and Development Authority ("BARDA") of up to $44.2 million to develop tebipenem HBr for the treatment of cUTI caused by antibiotic resistant Gram-negative bacteria and for assessment against biodefense pathogens. The award committed initial funding of $15.7 million over a three-year base period from July 1, 2018 to June 30, 2021 for cUTI development activities. In May 2019, the contract was modified to include additional funding of approximately $2.5 million for the development of tebipenem HBr, increasing the amount of the initial committed funding from $15.7 million to approximately $18.2 million and increasing the overall potential award to $46.8 million. In January 2020, BARDA exercised its first contract option for additional committed funding of $15.9 million, increasing the total committed funding to $34.0 million and extended the period of performance through November 1, 2021. In October 2021, BARDA extended the period of performance for the first contract option through December 15, 2022. As of December 31, 2021, the balance of the award was subject to BARDA exercising a second option which would entail funding of $12.7 million and is exercisable by BARDA subject to, among other things, satisfactory progress and results from the biodefense studies described below. On January 19, 2022, the Company announced that BARDA exercised a new option under the contract. The new option increases the total amount of committed funding by $12.9 million to approximately $46.9 million, increasing the total potential contract value to $59.7 million. The additional $12.9 million option is expected to provide support for a clinical trial and related activities for orally administered tebipenem HBr's use in treating pediatric patients with cUTIs, including acute pyelonephritis.

As part of an inter-agency collaboration between BARDA and the Defense Threat Reduction Agency ("DTRA"), a series of studies to assess the efficacy of tebipenem HBr in the treatment of infections caused by biodefense threats such as anthrax, plague and melioidosis will be conducted under the direction of Spero. DTRA provides up to $10.0 million, in addition to the total potential award from BARDA, to cover the cost of the nonclinical biodefense aspects of the collaborative program for tebipenem HBr. Together, BARDA and DTRA will provide up to $69.7 million in total funding for the clinical development and biodefense assessment of tebipenem HBr, of which $12.7 million is subject to the exercise of options by BARDA and Spero's achievement of specified milestones.

The Company recognized $0.7 million and $6.3 million of revenue under the BARDA award during the three months ended March 31, 2022 and 2021, respectively.

U.S. Department of Defense

On July 1, 2019, the Company received a $5.9 million award from the U.S. Department of Defense ("DoD") Congressionally Directed Medical Research Programs ("CDMRP") Joint Warfighter Medical Research Program. The funding will support the further clinical development of SPR206. The award commits non-dilutive funding of $5.9 million over a four-year period to cover the costs of select Phase 1 pharmacology studies, a 28-day GLP NHP toxicology study, and microbiological surveillance studies that would be required for a potential NDA submission with the FDA for SPR206. During the three months ended March 31, 2022 and 2021, the Company recognized $0.9 million and $0.6 million in revenue under this agreement, respectively.

NIAID

In May 2021, the Company was awarded a five-year contract from the U.S. National Institute of Allergy and Infectious Diseases ("NIAID") under the Agency's Omnibus Broad Agency Announcement No. HHS-NIH-NIAID-BAA2020-1 award mechanism to support further development of SPR206. Funding will be used to offset certain expenses related to manufacturing, clinical, non-clinical and regulatory activities. The Company can receive up to $23.4 million over a base period and five option periods. As of March 31, 2022, funding for the base period totaling $2.1 million has been committed. The Company recognized $0.3 million under this agreement during the three months ended March 31, 2022.

In June 2016, the Company entered into agreements with Pro Bono Bio PLC ("PBB"), a corporation organized under the laws of England, and certain of its affiliates, including PBB Distributions Limited and Cantab Anti-Infectives Limited ("CAI"), in order to acquire certain intellectual property and government funding arrangements relating to SPR206. Under these agreements, CAI agreed to submit a request to NIAID to novate the then CAI-held NIAID contract to Spero, which was finalized in December 2017. The NIAID contract provides for development funding of up to $6.5 million over a base period and three option periods. As of December 31, 2021, funding for the base period and the first two option periods totaling $5.9 million had been committed. In March 2021, a contract modification was executed and the performance period for this award was extended until June 15, 2021. The Company did not recognize revenue under this agreement during the three months ended March 31, 2022 and recognized $0.4 million during the three months ended March 31, 2021.

9. License, Collaboration and Service Agreements

The Company has certain obligations under license agreements with third parties that include annual maintenance fees and payments that are contingent upon achieving various development, regulatory and commercial milestones. Pursuant to these license agreements, the Company is required to make milestone payments if certain development, regulatory and commercial milestones are achieved, and may have certain additional research funding obligations. Also, pursuant to the terms of each of these license

agreements, when and if commercial sales of a product commence, the Company will pay royalties to its licensors on net sales of the respective products.

Cantab License Agreements

Under the Cantab Agreements, the Company is obligated to make future milestone payments of up to $5.8 million upon the achievement of specified clinical and regulatory milestones and a payment of £5.0 million ($6.6 million as of March 31, 2022) upon the achievement of a specified commercial milestone. In addition, the Company agreed to pay to PBB royalties, on a product-by-product and country-by-country basis, of a low single-digit percentage based on net sales of products licensed under the agreement. During both the three months ended March 31, 2022 and 2021, the Company did not record any research and development expense related to the achievement of regulatory milestones for SPR206.

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

Vertex License Agreement

In May 2016, the Company entered into an agreement with Vertex Pharmaceuticals Incorporated ("Vertex") whereby Vertex granted the Company certain know-how and a sublicense to research, develop, manufacture and sell products for a proprietary compound, as well as a transfer of materials. In exchange for the know-how, sublicense and materials, Spero paid Vertex an upfront, one-time, nonrefundable, non-creditable fee of $0.5 million, which was recognized as research and development expense. As part of the agreement, the Company is obligated to make future milestone payments of up to $80.2 million upon the achievement of specified clinical, regulatory and commercial milestones and to pay Vertex tiered royalties, on a product-by-product and country-by-country basis, of a mid-single-digit to low double-digit percentage based on net sales of products licensed under the agreement. During the three months ended March 31, 2022 and 2021, the Company did not record any research and development expense related to the achievement of regulatory milestones for SPR720 and the next milestone under this agreement is not accrued because it is not yet probable.

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

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. In October 2017, the Company paid a $1.0 million milestone payment to Meiji upon the enrollment of the first patient in the Company's Phase 1 clinical trial of tebipenem HBr. The payment was recorded as research and development expense in the statement of operations and comprehensive loss for the year ended December 31, 2017. The Company paid Meiji approximately $1.6 million during the fourth quarter of 2018 related to fixed assets which will be used in manufacturing related activities at Meiji. This equipment has been capitalized as property and equipment in the consolidated balance sheet as of March 31, 2022. In October 2021, the Company paid a $1.0 million milestone payment to Meiji upon submission of an NDA to the FDA for tebipenem HBr. As part of the agreement, the Company is obligated to make future milestone payments of up to $1.0 million as of March 31, 2022 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.

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

Everest Medicines License Agreement

On January 4, 2019, the Company, through its wholly owned subsidiary New Pharma License Holdings Limited ("NPLH"), entered into a license agreement (the "Original Everest License Agreement"), with Everest Medicines II Limited ("Everest"). Under the terms of the Original Everest License Agreement, the Company granted Everest an exclusive license to develop, manufacture and

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

Under the terms of the Original Everest License Agreement, the Company received an upfront payment of $3.0 million that was recognized in the first quarter of 2019, comprised of a $2.0 million payment to license SPR206 and $1.0 million for the exclusive option to negotiate a license to develop SPR741. The Company also received a milestone payment of $2.0 million in the fourth quarter of 2020 upon completion and delivery of the results of a clinical study.

On January 15, 2021, the Company entered into an amended and restated license agreement ("the Amended Everest License Agreement") with Everest and Spero Potentiator, Inc., which amended and restated in its entirety the Original Everest License Agreement. The Amended Everest License Agreement modifies the dates and values of certain milestone events related to development and commercialization of SPR206. Everest will now be making more significant investments in the development of SPR206 beyond what was contemplated at the time of the Original Everest License Agreement. The Original Everest License Agreement provided that the Company could receive up to $59.5 million upon achievement of certain milestones. The Amended Everest License Agreement provides that the Company may receive up to $38.0 million upon achievement of certain milestones, of which $1.3 million has been received to date. The Company may receive milestones of up to $1.5 million if the Company chooses to complete a future clinical study, of which the Company received approximately $0.8 million upon the initiation of the Bronchoalveolar Lavage ("BAL") clinical trial of SPR206 in June 2021 and will receive the remaining $0.7 million upon the delivery of a clinical study report. In addition, under the Amended Everest License Agreement, the Company assigned patents in the Territory to Everest, rather than licensing such patents to Everest, and the option related to SPR741 and the related provisions have been removed. Under the terms of the Amended Everest License Agreement, the Company is also entitled to receive high single-digit to low double-digit royalties on net sales, if any, of Licensed Products in the Territory following regulatory approval of SPR206. Everest has the right to sublicense to affiliates and third parties in the Territory.

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

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

During both the three months ended March 31, 2022 and 2021, the Company did not recognize any revenue related to this agreement.

Gates MRI Collaboration Agreement

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

The Company did not record a reduction to research and development expense as no activities were funded by Gates MRI during the three months ended March 31, 2022. The Company recorded $0.6 million as a reduction to research and development expense related to activities funded by Gates MRI during the three months ended March 31, 2021.

Savior Service Agreement

In November 2018, the Company entered into a service agreement with Savior Lifetec Corporation ("Savior") to perform technology transfer, process development, analytical method development and testing and formulation development for tebipenem HBr. Per the terms of the agreement, the Company paid Savior a non-refundable supervision fee of approximately $2.0 million to manage the buildout of a commercial manufacturing facility. The supervision fee was classified as a prepaid asset on the Company's balance sheet and was fully amortized over a service period of approximately 34 months as of December 31, 2021. The Company has paid Savior an additional $5.2 million for facility build out costs, which is classified as a long-term asset on the Company's balance sheet as of March 31, 2022.

Pfizer License and Share Purchase Agreements

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

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

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

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

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

Accounting Analysis and Revenue Recognition

The Company determined that Pfizer is a customer and that the Pfizer License Agreement is within the scope of ASC 606 as licensing intellectual property and performing ongoing research and development services are ordinary activities that are ongoing and central to the Company's operations. Accordingly, in determining the appropriate amount of revenue to be recognized, the Company performed the following steps: (i) identified the promised goods or services in the contract; (ii) determined whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measured the

transaction price, including the constraint on variable consideration; (iv) allocated the transaction price to the identified performance obligations in proportion to their SSP; and (v) recognized revenue when each performance obligation was deemed to be satisfied.

Based on that evaluation, the Company identified two performance obligations, as presented below. The Company determined that the supply agreement is a customer option and not a material right, as the pricing to Pfizer is not at a significant discount. Furthermore, Pfizer has the right to use third parties to manufacture the compound, or to manufacture the compound itself. The transaction price to be allocated to the identified performance obligations was determined to be the $12.5 million premium on the Company's commitment to sell common stock to Pfizer under the Pfizer Purchase Agreement at a price per share in excess of fair value. The allocation was performed based on the relative standalone selling prices of the performance obligations. The following table shows the performance obligations and the transaction price allocated to those obligations (in millions):

Performance Obligations	Transaction Price Allocated	Recognition Method
License and know-how transfer (1)	$ 1.4	Fully satisfied; recognized upon delivery of the license
Research and development services related to upcoming milestones (2)	11.1	Recognized over time as services are delivered
	$ 12.5	

1. The standalone selling price for the license and know-how was determined by the income approach utilizing a discounted cash flow. The key assumptions in the Company's estimate of the standalone selling price for the license and know-how include the probability of technological and regulatory success, an estimate of future product revenues, and the discount rate, among others.
2. The standalone selling price for the research and development services was estimated based on the Company's estimate of costs to be incurred to fulfill its obligations associated with the performance of the research and development services, plus a reasonable margin.

The potential license maintenance fees and development milestone payments from the Pfizer License Agreement will be accounted for as variable consideration under ASC 606. Given the uncertain nature of these payments, the Company determined they were fully constrained as of March 31, 2022 and not included in the transaction price. The Company can also earn sales-based royalties.

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

The Company recognized $0.2 million of revenue from the contract during the three months ended March 31, 2022. The remaining transaction price balance of approximately $10.4 million from the Pfizer Purchase Agreement allocated to the research and development services performance obligation has been recorded as deferred revenue in the condensed consolidated balance sheet. As of March 31, 2022, the research and development services related to the second performance obligation were expected to be recognized as costs are incurred over the project development timeframe.

10. Liability Related to the Sale of Future Royalties

On September 29, 2021, the Company entered into a Revenue Interest Agreement with certain entities managed by HealthCare Royalty Management, LLC (“HCR”), pursuant to which the Company sold to HCR the right to receive certain royalty payments from the Company for a purchase price of up to $125.0 million. The Company has evaluated the terms of the Revenue Interest Agreement and concluded that the features of the investment amount are similar to those of a debt instrument. The Company received gross proceeds of $50.0 million from HCR at an initial funding on October 19, 2021 (the “Initial Investment Amount”). As such, the Company accounted for this transaction as long-term debt as of December 31, 2021. The Company is entitled to receive an additional $50.0 million upon FDA approval of tebipenem HBr on or before December 31, 2022 (the “Second Investment Amount”), and an additional $25.0 million subject to the mutual agreement of the Company and HCR and if the Company meets certain minimum tebipenem HBr product sales thresholds in the United States within 12 months from commercial launch (the “Third Investment Amount,” and together with the Initial Investment Amount and the Second Investment Amount, collectively, the “Investment Amount”).

Under the Revenue Interest Agreement, HCR is entitled to receive tiered royalties on: (i) worldwide net sales of Included Products (as defined below) by the Company (and excluding sales by licensees), and (ii) any payments received by licensees, in each case of tebipenem HBr, SPR720, SPR206 and any other products marketed by the Company (the "Included Products") in amounts ranging from 12% to 1% based on annual net revenues (or 14% to 1.5% if the Third Investment Amount is funded). The applicable royalty rate is subject to a step-down if certain sales milestones are met. When HCR has received aggregate payments equal to 250% of the Investment Amount (the "Hard Cap"), HCR's right to receive royalties on Net Revenues will terminate. The Hard Cap will be $250 million upon tebipenem HBr approval, or $312.5 million if the Third Investment Amount is funded.

If the Company has not received FDA approval for tebipenem HBr for a cUTI indication on or prior to December 31, 2022, the Revenue Interest Agreement will terminate and the Company will pay to HCR, no later than January 15, 2023, an amount equal to the Initial Investment Amount plus interest equal to an annual 13.5% rate of return.

If HCR has not received aggregate payments of at least 60% of the Investment Amount by September 30, 2025 and at least 100% of the Investment Amount by September 30, 2027 (each, a "Minimum Amount"), then the Company will be obligated to make a cash payment to HCR in an amount sufficient to gross HCR up to the applicable Minimum Amount.

At inception of the Revenue Interest Agreement, the Company accounted for the transaction as long-term debt and as short-term debt as of March 31, 2022. The gross proceeds of the Initial Investment Amount of $50.0 million were recorded as a liability related to the sale of future royalties, net of transaction costs of $2.5 million and initial derivative liability of $1.0 million, which will be amortized over the estimated life of the arrangement using the effective interest method. The fair value for the liability related to the sale of future royalties at the time of the transaction was based on the Company's current estimates of future royalties expected to be paid to HCR over the remaining patent life of the product, which are considered Level 3 inputs.

The Company estimates the effective interest rate used to record non-cash interest expense under the Revenue Interest Agreement based on the estimate of future royalty payments to be received by HCR. As of March 31, 2022, the estimated effective interest rate under the agreement was 20.8%. Over the life of the arrangement, the actual effective interest rate will be affected by the amount and timing of the royalty payments received by HCR and changes in the Company's forecasted royalties. At each reporting date, the Company will reassess its estimate of total future royalty payments to be received by HCR, and prospectively adjust the effective interest rate and amortization of the liability as necessary.

In connection with the initial investment amount, the Company classified $1.0 million at inception of the Revenue Interest Agreement as a derivative liability on its consolidated balance sheet because there were embedded instruments that represent a conditional obligation to pay HCR the final payment, which is 250% of the Investment Amount, upon an event of default or change of control (see Note 3).

The following table presents the changes in the liability related to the sale of future royalties under the Revenue Interest Agreement with HCR as of March 31, 2022 (in thousands):

Liability related to sale of future royalties, as of December 31, 2021	$	48,414
Plus Interest expense accrued/ recognized		2,488
Liability related to sale of future royalties, as of March 31, 2022	$	50,902

11. 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 during both the three months ended March 31, 2022 and 2021, respectively, to research and development expenses in the consolidated statements of operations and comprehensive loss associated with this tax incentive, representing 43.5% of the Company's qualified research and development spending in Australia. The 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 $0.4 million and $0.4 million as of March 31, 2022, and December 31, 2021, respectively.

12. 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,	
	2022	2021
Numerator:		
Net loss	$ (32,829)	$ (19,423)
Net loss attributable to common stockholders	$ (32,829)	$ (19,423)
Denominator:		
Weighted average common shares outstanding, basic and diluted	32,606,715	29,414,148
Net loss per share, basic and diluted	$ (1.01)	$ (0.66)

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,	
	2022	2021
Options to purchase common stock	5,775,068	4,583,140
Unvested restricted stock units	1,163,647	—
Series B convertible preferred stock (as converted to common shares)	938,000	938,000
Series C convertible preferred stock (as converted to common shares)	2,214,000	2,214,000
Series D convertible preferred stock (as converted to common shares)	3,215,000	3,215,000
	13,305,715	10,950,140

13. Subsequent Events

On May 3, 2022, the Company announced that it would immediately suspend current commercialization activities for tebipenem HBr based on feedback from a recent Late Cycle Meeting ("LCM") with the FDA regarding the Company's NDA for tebipenem HBr. Although the review is still ongoing and the FDA has not yet made any final determination regarding approvability, the discussion suggested that the data package may be insufficient to support approval during this review cycle. As a result, the Company has restructured its operations to focus on advancing its earlier stage programs, SPR720 and SPR206, while it continues its dialogue with the FDA to seek a pathway forward for the potential approval of tebipenem HBr.

In connection with the foregoing, on May 3, 2022, the Company implemented a strategic restructuring initiative and corresponding reduction in workforce The restructuring initiative and corresponding reduction in workforce is designed to reduce costs and reallocate resources towards the Company's clinical development programs for SPR720 and SPR206, while maintaining key personnel needed to help preserve the value of the Company's tebipenem HBr program. The restructuring reduced the Company's workforce from 146 full-time employees as of December 31, 2021 to approximately 35 full-time employees. The Company estimates that it will incur approximately $8.0 million of costs in connection with the reduction in workforce related to severance pay and other related termination benefits. The Company communicated the workforce reduction on May 3, 2022 and expects the majority of the costs associated with the restructuring to be incurred during the quarter ending June 30, 2022.

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, 2021. 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 bacterial infections, including MDR bacterial infections, and rare diseases. Our most advanced product candidate, tebipenem HBr, is designed to be the first broad-spectrum oral carbapenem-class antibiotic for use to treat certain bacterial infections that cause complicated urinary tract infections ("cUTIs"), including pyelonephritis, caused by certain microorganisms, in adult patients who have limited oral treatment options. Treatment with effective orally administrable antibiotics may prevent hospitalizations for serious infections and enable earlier and cost-effective treatment of patients after hospitalization. We are also developing SPR720, a novel oral antibiotic designed for the treatment of a rare, orphan disease caused by non-tuberculous mycobacterial pulmonary infections ("NTM"). We are continuing to engage with the FDA on specifics of the upcoming SPR720 Phase 2 clinical trial, which we expect to begin in the second half of 2022, with an expected interim data read-out in 2023 and topline results in 2024. In addition, we are developing an IV-administered product candidate, SPR206, to treat MDR Gram-negative infections in the hospital. We believe that our novel product candidates, if successfully developed and approved, would have meaningful patient impacts and significant commercial applications for the treatment of bacterial infections, including MDR infections, in both the community and hospital settings. Since our inception in 2013, we have focused substantially all of our efforts and financial resources on organizing and staffing our company, business planning, raising capital, acquiring and developing product and technology rights, building our intellectual property portfolio and conducting research and development activities for our product candidates. We do not have any products approved for sale and have not generated any revenue from product sales.

We have experienced net losses and significant cash outflows from cash used in operating activities since our inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. As of March 31, 2022, we had an accumulated deficit of $400.3 million, and cash, cash equivalents and marketable securities of $122.0 million. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. Based on our announced strategic restructuring described below and the cessation of commercialization activities for the tebipenem HBr program and assuming the repayment of amounts under our Revenue Interest Financing Agreement with certain entities managed by HealthCare Royalty Management, LLC, we believe that our existing cash, cash equivalents and marketable securities, together with other non-dilutive funding commitments, will be sufficient to fund our planned operating expenses and capital expenditures pursuant to the priorities of our strategic refocusing through late 2023. During this period, our announced strategic refocusing described below prioritizes advancing SPR720 and SPR206 to key Phase 2 milestones. For more information, see Note 10 - Liability Related to the Sale of Future Royalties to the Financial Statements. This timeline is subject to uncertainty as to the timing of future expenditures. We have developed plans to mitigate this risk, which primarily consist of raising additional capital through some combination of equity or debt financings, potential new collaborations, additional grant funding and/or reducing cash expenditures. If we are not able to secure adequate additional funding, we plan to make reductions in spending. In that event, we may have to delay, scale back, or eliminate some or all of our planned clinical trials and research stage programs. The actions necessary to reduce spending under this plan at a level that mitigates the factors described above is not considered probable, as defined in the accounting standards and therefore, the full extent to which management may extend our funds through these actions may not be considered in management's assessment of our ability to continue as a going concern. As a result, management has concluded that substantial doubt exists about our ability to continue as a going concern.

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

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

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

Recent Developments

On May 3, 2022, we announced that we would immediately suspend current commercialization activities for tebipenem HBr based on feedback from a recent Late Cycle Meeting ("LCM") with the FDA regarding our NDA for tebipenem HBr. Although the review is still ongoing and the FDA has not yet made any final determination regarding approvability, the discussion suggested that the data package may be insufficient to support approval during this review cycle. As a result, we have restructured our operations to focus on advancing our earlier stage programs, SPR720 and SPR206, while we continue our dialogue with the FDA to seek a pathway forward for the potential approval of tebipenem HBr. We believe this re-prioritized strategic focus is the best way to optimize our financial and other resources to advance our goal of developing and commercializing product candidates to address the unmet need for solutions to antibiotic resistant pathogens.

In connection with the foregoing, on May 3, 2022, we implemented a strategic restructuring initiative and corresponding reduction in workforce The restructuring initiative and corresponding reduction in workforce is designed to reduce costs and reallocate resources towards our clinical development programs for SPR720 and SPR206, while maintaining key personnel needed to help preserve the value of our tebipenem HBr program. The restructuring reduced our workforce from 146 full-time employees as of December 31, 2021 to approximately 35 full-time employees. We estimate that we will incur approximately $8.0 million of costs in connection with the reduction in workforce related to severance pay and other related termination benefits. We communicated the workforce reduction on May 3, 2022 and expect the majority of the costs associated with the restructuring to be incurred during the quarter ending June 30, 2022.

Components of our Results of Operations

Sales Revenue

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

Grant Revenue

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

Collaboration Revenue

Collaboration revenue relates to our agreements with Everest and Pfizer.

Operating Expenses

Research and Development Expenses

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

- employee-related expenses, including salaries, related benefits, travel and share-based compensation expense for employees engaged in research and development functions;
- expenses incurred in connection with the preclinical and clinical development of our product candidates, including under agreements with contract research organizations ("CROs");
- costs incurred in connection with our government awards;
- the cost of consultants and contract manufacturing organizations ("CMOs") that manufacture drug products for use in our preclinical studies and clinical trials;

- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and supplies; and
- payments made under third-party licensing agreements.

We have recorded research and development expenses conducted by our Australian subsidiary net of a 43.5% research and development tax incentive we expect to receive for qualified expenses from the Australian government.

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

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

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

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

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

- successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority, including on account of the disruptive impacts of the COVID-19 pandemic;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers to obtain manufacturing supply;
- obtainment and maintenance of patent, trade secret protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain our license agreement with Meiji with respect to tebipenem HBr;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales of our product candidates, if approved, whether alone or in collaboration with others;
- acceptance of our product candidates, if approved, by patients, the medical community and third-party payors;
- competition with other therapies; and
- a continued acceptable safety profile of our product candidates, if approved.

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

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs, including share-based compensation, for personnel in executive, finance and administrative functions. General and administrative expenses also include direct and allocated facility-related costs as well as professional fees for legal, patent, consulting, investor and public relations, accounting and audit services.

In light of our decision to suspend current commercialization activities for tebipenem HBr and our strategic restructuring, we expect that our future expected general and administrative expenses relating to commercialization activities will be substantially reduced. We currently expect our general and administrative expenses to be lower for the remainder of 2022 as we progress through our discussions with the FDA regarding the NDA for tebipenem HBr and implement our restructuring. In connection with our restructuring, we estimate that we will incur approximately $8.0 million of costs in connection with the reduction in workforce related to severance pay and other related termination benefits. We expect the majority of the costs associated with our restructuring to be incurred during the quarter ending June 30, 2022. We also anticipate that we will continue to incur accounting, audit, legal, regulatory, compliance, infrastructure and director and officer insurance costs as well as investor and public relations expenses associated with our continued operation as a public company.

Other Income (Expense)

Interest Income (Expense)

Interest income (expense) consists of interest expense related to the sale of future royalties and interest earned on our cash equivalents, which are primarily invested in money market accounts, as well as interest earned on our investments in marketable securities that we held during the three months ended March 31, 2022 and 2021.

Other Income (Expense), Net

Other income (expense), net, consists of insignificant amounts of miscellaneous income, as well as the change in the fair value of our derivative liability, realized and unrealized gains and losses from foreign currency-denominated cash balances, vendor payables and receivables from the Australian research and development tax incentive.

Critical Accounting Policies and Significant Judgments and Estimates

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

We have made no changes to our existing critical accounting policies, as described in our Annual Report on Form 10-K for the year ended December 31, 2021.

Results of Operations

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

Comparison of the Three Months Ended March 31, 2022 and 2021

The following table summarizes our results of operations for the three months ended March 31, 2022 and 2021 (in thousands):

	Three Months Ended March 31,		
	2022	2021	$ Change
Revenues:			
Grant revenue	$ 1,822	$ 7,300	$ (5,478)
Collaboration revenue	247	—	247
Total revenues	2,069	7,300	(5,231)
Operating expenses:			
Research and development	16,971	18,404	(1,433)
General and administrative	15,305	8,299	7,006
Total operating expenses	32,276	26,703	5,573
Loss from operations	(30,207)	(19,403)	(10,804)
Other income (expense):			
Interest income	72	98	(26)
Other income (expense), net	(13)	(118)	105
Interest expense related to the sale of future royalties	(2,488)	—	(2,488)
Change in fair value of derivative liability	(193)	—	(193)
Total other income (expense), net	(2,622)	(20)	(2,602)
Net loss	$ (32,829)	$ (19,423)	$ (13,406)

Grant Revenue

	Three Months Ended March 31,		
	2022	2021	$ Change
BARDA Contract (tebipenem HBr)	$ 675	$ 6,296	$ (5,621)
NIAID Contract (SPR206)	253	359	(106)
DoD Agreement (Potentiator product candidate)	894	645	249
Total grant revenue	$ 1,822	$ 7,300	$ (5,478)

Grant revenue recognized during the three months ended March 31, 2022 and 2021 consisted of the reimbursement of qualifying expenses incurred in connection with our various government awards. The decrease in revenue during the three months ended March 31, 2022 was primarily due to a $5.6 million decrease in qualified expenses incurred under our BARDA contract for tebipenem HBr and a $0.1 million decrease in funding under our NIAID agreement relating to SPR206, partially offset by an increase of $0.2 million under our DoD agreement relating to SPR206.

Collaboration Revenue

During the three months ended March 31, 2022, we recognized $0.2 million in collaboration revenue related to our agreement with Pfizer. During the three months ended March 31, 2021, we did not recognize any collaboration revenue, as the aggregate amount of the transaction price related to our agreement with Everest was fully allocated to satisfied performance obligations in prior periods and we did not enter into our agreement with Pfizer until June 30, 2021.

Research and Development Expenses

	Three Months Ended March 31,		
	2022	2021	$ Change
Direct research and development expenses by program:			
Tebipenem HBr	$ 6,244	$ 10,115	$ (3,871)
SPR720	85	1,243	(1,158)
Potentiator product candidate (SPR206)	1,920	1,090	830
Unallocated expenses:			
Personnel related (including share-based compensation)	7,513	4,752	2,761
Facility related and other	1,209	1,204	5
Total research and development expenses	$ 16,971	$ 18,404	$ (1,433)

Direct costs related to our tebipenem HBr program decreased by $3.9 million during the three months ended March 31, 2022 compared to the three months ended March 31, 2021, primarily due to the completion of significant activities to support our NDA for tebipenem HBr. We expect to continue to incur some direct costs related to tebipenem HBr as we perform ongoing activities to support the further development of tebipenem HBr.

Direct costs related to our SPR720 program decreased by $1.2 million during the three months ended March 31, 2022 as compared to the three months ended March 31, 2021, primarily due to the clinical hold placed on our Phase 2a clinical trial of SPR720. In January 2022, we announced the FDA lifted the clinical hold on the Phase 2 trial of SPR720. We expect to continue to incur direct costs related to SPR720 as we progress preclinical and clinical activities. Direct costs related to our SPR720 program during the three months ended March 31, 2021 reflect a $0.6 million reduction to expense related to activities funded by Gates MRI.

Direct costs related to our SPR206 program increased by $0.8 million during the three months ended March 31, 2022, primarily due to higher clinical costs.

During 2022 and 2021, research and development expenses incurred by our Australian subsidiary were recorded net of a 43.5% research and development tax incentive for qualified expenses from the Australian government, resulting in a receivable of $0.4 million as of March 31, 2022.

The increase in personnel-related costs of $2.8 million was primarily a result of an increase in research and development headcount. Personnel-related costs for the three months ended March 31, 2022 and 2021 included share-based compensation expense of $1.4 million and $0.8 million, respectively.

During the three months ended March 31, 2022 and 2021, facility-related and other costs were primarily flat and reflect costs related to supporting our research and development staff.

General and Administrative Expenses

	Three Months Ended March 31,		
	2022	2021	$ Change
Personnel related (including share-based compensation)	$ 8,442	$ 4,429	$ 4,013
Professional and consultant fees	5,648	3,112	2,536
Facility related and other	1,215	758	457
Total general and administrative expenses	$ 15,305	$ 8,299	$ 7,006

The increase in personnel-related costs of $4.0 million was primarily a result of an increase in headcount in our commercial, general and administrative functions. Personnel-related costs for the three months ended March 31, 2022 and 2021 included share-based compensation expense of $1.8 million and $1.2 million, respectively.

The increase in professional and consultant fees of $2.5 million was primarily due to increased commercial operation expenses to support the potential commercialization of tebipenem HBr, as well as increased legal and consulting expenses.

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

Other Income (Expense), Net

Other expense, net was $(2.6) million for the three months ended March 31, 2022, compared to less than $(0.1) million for the three months ended March 31, 2021. Total other expense for the three months ended March 31, 2022 included $2.5 million in interest expense related to the sale of future royalties, a $0.2 million increase in our derivative liability and net immaterial changes primarily due to fluctuations in unrealized foreign currency gains, offset by interest income.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We have recognized limited revenue to date from funding arrangements with the DoD, NIAID, CARB-X and BARDA and our license agreements with Everest and Pfizer. We have not yet commercialized any of our product candidates and we may not generate revenue from sales of any product candidates. To date, we have funded our operations with payments received under license and collaboration agreements and funding from government contracts, and mostly from the proceeds of multiple common stock offerings. In addition, in September 2021, we entered into our Revenue Interest Agreement. As of March 31, 2022, we had cash, cash equivalents and marketable securities of $122.0 million.

On March 11, 2021, we entered into a new sales agreement with Cantor and filed a new universal shelf registration statement on Form S-3 (Registration No. 333-254170), pursuant to which we registered for sale up to $300.0 million of any combination of our common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that we may determine, including up to $75.0 million of our common stock available for issuance pursuant to the new “at-the-market” offering program sales agreement that we entered into with Cantor. Under the new 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 new sales agreement. Our universal shelf registration statement on Form S-3 (Registration No. 333-254170) became effective on March 29, 2021 and our prior sales agreement with Cantor terminated automatically at such time.

During the three months ended March 31, 2022, we sold 344,205 shares of our common stock under our "at-the-market" agreements at an average price of approximately $10.86 per share for aggregate gross proceeds of approximately $3.7 million prior to deducting sales commissions.

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

Cash Flows

The following table summarizes our sources and uses of cash for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,	
	2022	2021
Cash used in operating activities	$ (28,223)	$ (15,479)
Cash provided by investing activities	(16,064)	3,003
Cash provided by financing activities	3,814	4,309
Net increase in cash and cash equivalents	$ (40,473)	$ (8,167)

Operating Activities

Net cash used in operating activities for the three months ended March 31, 2022 was $28.2 million, primarily resulting from our net loss of $32.8 million, adjusted for net decrease in non-cash items of $6.3 million (primarily stock-based compensation, interest expense associated with the sale of future royalties, depreciation and amortization). Net cash used due to changes in our operating assets and liabilities was $1.7 million and consisted primarily of a $0.2 million decrease in deferred revenue, $0.7 million net decrease in receivables, a decrease of $5.3 million in accrued expenses, and a $3.7 million increase in accounts payable.

Net cash used in operating activities for the three months ended March 31, 2021 was $15.5 million, primarily resulting from our net loss of $19.4 million, adjusted for net non-cash items of $2.4 million (primarily stock-based compensation, depreciation and amortization). Net cash provided by changes in our operating assets and liabilities was $1.5 million and consisted primarily of a $2.7 million increase in accounts payable, a $2.4 million net increase in receivables, a $0.9 million decrease in prepaid expenses and other current assets and an increase of $0.6 million in accrued expenses.

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

Investing Activities

Cash used by investing activities during the three months ended March 31, 2022 was $16.1 million primarily related to the maturities of marketable securities of $10.9 million, offset by purchases of marketable securities of $27.0 million.

Cash provided by investing activities during the three months ended March 31, 2021 was $3.0 million primarily related to the maturities of marketable securities of $6.0 million, offset by purchases of marketable securities of $3.0 million.

Financing Activities

Cash provided by financing activities during the three months ended March 31, 2022 was $3.8 million, and consisted primarily of $3.6 million net sales of common stock under our "at-the-market" offering program sales agreement and proceeds of $0.2 million from the exercise of employee stock options.

Cash provided by financing activities during the three months ended March 31, 2021 was $4.3 million, and consisted primarily of $4.3 million net sales of common stock under our "at-the-market" offering program sales agreement and proceeds of $0.1 million from the exercise of employee stock options, offset by the payment of offering expenses of less than $0.1 million.

Funding Requirements

Our future use of operating cash and capital requirements, and the timing and amount thereof, will depend largely on:

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

As of March 31, 2022, we had cash, cash equivalents and marketable securities of $122.0 million. In accordance with ASU 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40), we are required to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern from the issuance date of our financial statements. Based on our announced strategic restructuring and the cessation of commercialization activities for the tebipenem HBr program and assuming the repayment of amounts under our Revenue Interest Financing Agreement with certain entities managed by HealthCare Royalty Management, LLC, we believe that our existing cash, cash equivalents and marketable securities, together with other non-dilutive funding commitments, will be sufficient to fund our planned operating expenses and capital expenditures pursuant to the priorities of our strategic refocusing through late 2023. For more information, see Note 10 - Liability Related to the Sale of Future Royalties to the Financial Statements.

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

Our consolidated financial statements as of December 31, 2021 were prepared under the assumption that we will not continue as a going concern for the next twelve months. As a result, the opinion from our independent registered public accounting firm with respect to our annual financial statements contains an explanatory paragraph about such substantial doubt about our ability to continue as a going concern. Our ability to continue as a going concern is dependent upon our ability to obtain additional equity or debt financing, attain further operating efficiencies, reduce expenditures, and, ultimately, to generate revenue. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. The substantial doubt about our ability to continue as a going concern may adversely affect our stock price and our ability to raise capital. There is no assurance that we will be successful in obtaining sufficient funding on acceptable terms, if at all, and we could be forced to delay, reduce or eliminate some or all of our research and development programs, product portfolio expansion or commercialization efforts, which could materially adversely affect our business prospects or our ability to continue operations.

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

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

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of equity offerings, debt financings, government funding, collaborations, strategic alliances and marketing, distribution or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions or capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. The COVID-19 pandemic has resulted in ongoing volatility in financial markets. If our access to capital is restricted or associated borrowing costs increase as a result of developments in financial markets, including relating to the COVID-19 pandemic, our operations and financial condition could be adversely impacted. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our research, product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

During the three months ended March 31, 2022, 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, 2021.

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, 2022, we had cash, cash equivalents and marketable securities of $122.0 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, 2022, the net fair value of our interest sensitive marketable securities would hypothetically decline by $0.1 million. As we incur research expenses in foreign countries, we face exposure to movements in foreign currency exchange rates, primarily the Euro, British Pound, Japanese Yen 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, 2022. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of March 31, 2022, 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(d) and 15d-15(d) under the Exchange Act) occurred during the three months ended March 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any material litigation.

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 Product Development and Commercialization

Pursuant to our recently announced restructuring, we have suspended all commercialization efforts with respect to tebipenem HBr and have shifted our focus and resources to advancing the clinical development of our other programs, SPR720 and SPR206, while continuing our dialogue with the FDA to seek a pathway forward for the potential approval of tebipenem HBr. If we fail to execute successfully on this re-prioritized strategic focus, our business and prospects may be adversely affected.

On May 3, 2022, we announced that we would immediately suspend current commercialization activities for tebipenem HBr based on feedback from a recent Late Cycle Meeting ("LCM") with the FDA regarding our NDA for tebipenem HBr. Although the review is still ongoing and the FDA has not yet made any final determination regarding approvability, the discussion suggested that the data package may be insufficient to support approval during this review cycle. As a result, we have restructured our operations to focus on advancing our earlier stage programs, SPR720 and SPR206, while we continue our dialogue with the FDA to seek a pathway forward for the potential approval of tebipenem HBr. We believe this re-prioritized strategic focus is the best way to optimize our financial and other resources to advance our goal of developing and commercializing product candidates to address the unmet need for solutions to antibiotic resistant pathogens. However, there is no assurance that we will be successful at executing on this strategy. As described below, there are risks inherent in the clinical development process, especially for earlier-stage programs, and the regulatory path for potential approval of tebipenem HBr remains uncertain at this time. If we are unable to execute successfully on this re-prioritized strategic focus, our business and prospects may be adversely affected.

Based on our recent feedback for the FDA, the timing and terms of any potential approval of tebipenem HBr remain uncertain, which may impact our ability to realize the value of tebipenem HBr.

We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of tebipenem HBr as a product candidate for the treatment of bacterial infections causing cUTI. Our ability to realize the value of tebipenem HBr depends on having a regulatory path for potential FDA approval, whose expected timeline and other requirements would affect the attractiveness of eventual commercialization of tebipenem HBr by us or commercialization through a potential partnership. However, the FDA has substantial discretion in reviewing the NDA for tebipenem HBr. There can be no assurances about the outcomes of our ongoing discussions with the FDA concerning our NDA for tebipenem HBr. The FDA may be unable to meet its PDUFA goal date for our NDA for tebipenem HBr; or it may request additional information from us in support of our NDA, the provision of which information could constitute a major amendment to the NDA and result in a three-month extension of the PDUFA date. The FDA may decline to approve the NDA and instead issue a complete response letter. Further, as part of any approval, the FDA could impose labeling requirements restricting the use of tebipenem HBr, which could reduce its commercial prospects, unless such requirements are subsequently modified to reduce such restrictions. If any of these outcomes occur, our business could be materially harmed.

If our clinical trials fail to produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.

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

The clinical development of any of our product candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to demonstrate efficacy in a trial or across a broad population of patients, the occurrence of severe adverse events, failure to comply with protocols or applicable regulatory requirements, and determination by the FDA or any comparable foreign regulatory authority that a drug product is not approvable. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in clinical trials, even after promising results in earlier nonclinical studies or clinical trials. The results of preclinical and other nonclinical studies and/or early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Notwithstanding any promising results in early nonclinical studies or clinical trials, we cannot be certain that we will not face similar setbacks.

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

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

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

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

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

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

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

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

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

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

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

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

- our ability to obtain and maintain patient consents; and
- the risk that participants enrolled in clinical trials will drop out of the trials before completion.

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

Separately, in response to the COVID-19 pandemic and public health emergency declaration in the United States, in March 2020, the FDA temporarily postponed most inspections of foreign manufacturing facilities and products. On March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and most inspections of foreign manufacturing facilities. The agency also provided guidance regarding the conduct of clinical trials during the COVID-19 pandemic, which has been updated periodically since that time with common questions and answers. Since that time, the FDA has developed a risk-based prioritization system for resuming on-site inspections, to be used for identifying the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities, based on local conditions and the prevalence of the virus. The FDA has also employed remote interactive evaluations and used alternative tools such as remote records requests, as outlined in its “Resiliency Roadmap for FDA Inspectional Oversight” that was first issued in May 2021 and updated in November 2021. Due to the rapid spread of the COVID-19 omicron variant at the end of 2021, the FDA announced certain inspections, such as domestic and foreign preapproval, surveillance, and for-cause inspections that are not deemed mission-critical, would be postponed through February 4, 2022, and that the agency would reassess plans to resume foreign inspections. However, the FDA has generally continued to ensure timely reviews of applications for prescription drug products during the COVID-19 pandemic in line with its user fee performance goals and conducting mission-critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards.

The FDA may not be able to maintain this pace and delays or setbacks are possible in the future.

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

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

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

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

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

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

Serious adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, an IRB, or regulatory authorities to interrupt, delay or halt our clinical trials and could result in a more restrictive label, the imposition of distribution or use restrictions or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. If any of our other product candidates are associated with serious or unexpected adverse events or undesirable side effects, the FDA, the IRBs 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.

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

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

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

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

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

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

- the efficacy and safety of the product candidate as demonstrated in clinical trials;
- relative convenience and ease of administration;

- the clinical indications for which the product candidate is approved;
- the potential and perceived advantages and disadvantages of the product candidates, including cost and clinical benefit relative to alternative treatments;
- the willingness of physicians to prescribe the product and of the target patient population to try new therapies;
- the willingness of hospital pharmacy directors to purchase the product for their formularies;
- acceptance by physicians, patients, operators of hospitals and treatment facilities and parties responsible for coverage and reimbursement of the product;
- the availability of coverage and adequate reimbursement by third-party payors and government authorities;
- the effectiveness of our sales and marketing efforts;
- the strength of marketing and distribution support;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling or an approved 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 of any of our product candidates that obtains regulatory approval to achieve market acceptance or commercial success would adversely affect our business prospects.

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

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

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

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

To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource those functions to third parties. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we intend to target. If we are unable to establish a sales force and marketing and distribution capabilities, our operating results may be adversely affected.

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

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;

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

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

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

There are also a number of oral product candidates in clinical development by third parties that are intended to treat cUTIs. One such product candidate is ceftibuten/clavulanate ("C-Scape") from Cipla Therapeutics, 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., imipenem/cilastatin and relebactam ("Recarbrio") from Merck & Co., plazomicin ("Zemdri") from Cipla Therapeutics, Inc., cefiderocol ("Fetroja") from Shionogi & Co. Ltd., eravacycline ("Xerava") from Tetraphase Pharmaceuticals, Inc. and meropenem-vaborbactam ("Vabomere") from Melinta Therapeutics, Inc.

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

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

Marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins

after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, which may negatively affect the revenues that we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the

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

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

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

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

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

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

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

In addition, the European Parliament and the Council of the European Union adopted a comprehensive general data privacy regulation ("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, including by companies outside of the European Union. The GDPR, which is wide-ranging in scope, imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, the security and confidentiality of the personal data, data breach notification and the use of third party processors in connection with the processing of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the United States, enhances enforcement authority and imposes large penalties for noncompliance, including the potential for fines of up to €20 million or 4% of the annual global revenues of the infringer, whichever is greater.

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

In addition, certain states have adopted privacy and security laws and regulations, some of which are more stringent than HIPAA and/or regulate information other than PHI. For example, in June 2018, California enacted the California Consumer Privacy Act ("CCPA") which took effect on January 1, 2020. The CCPA gives California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that may increase data breach litigation. Although the CCPA includes exemptions for certain clinical trials data, and HIPAA protected health information, the law may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. In addition, California voters also approved a new privacy law, the California Privacy Rights Act, ("CPRA"), on November 3, 2020. CPRA will modify CCPA significantly, potentially resulting in further uncertainty, additional costs and expenses stemming from efforts to comply, and additional potential for harm and liability for failure to comply. CPRA imposes additional obligations on companies covered by the legislation and will expand consumers' rights with respect to certain sensitive personal information CPRA also creates a new state agency that will be vested with the authority to implement and enforce CCPA and CPRA. CCPA has prompted a number of proposals for new federal and state privacy legislation that, if passed, could increase our potential liability, increase our compliance costs and adversely affect our business. For example, in February 2021, the Virginia legislature became the second to enact a state-specific law called the Consumer Data Protection Act ("CDPA"), which includes key differences from California's law, further complicating compliance by industry and other stakeholders. Many similar laws have been proposed in other states and at the federal level.

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

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

Risks Related to Our Financial Position and Need for Additional Capital

Our Revenue Interest Financing Agreement with HCR could limit cash flow available for our operations and expose us to risks that could adversely affect our business, financial condition and results of operations.

In exchange for the total investment amount received by us from HCR under our Revenue Interest Agreement, entered into on September 29, 2021, we must pay HCR a tiered royalty on applicable revenue generated by tebipenem HBr, SPR720 and SPR206 and other products marketed by us until the aggregate amount paid to HCR is two and a half times the total investment amount. We received gross proceeds of $50.0 million from HCR at an initial funding on October 19, 2021 (the "Initial Investment Amount"). We are entitled to receive an additional $50.0 million upon FDA approval of tebipenem HBr on or before December 31, 2022 (the "Second Investment Amount") and an additional $25.0 million subject to the mutual agreement of us and HCR and if we meet certain minimum tebipenem HBr product sales thresholds in the United States within 12 months from commercial launch (the "Third Investment Amount" and together with the Initial Investment Amount and the Second Investment Amount, collectively, the "Investment Amount"). Specifically, the tiered royalties are on: (1) worldwide net sales of Included Products (as defined below) by us (and excluding sales by licensees), and (2) any payments received by licensees, in each case of tebipenem HBr, SPR720, SPR206 and any other products marketed by us, which we refer to as the Included Products, in amounts ranging from 12% to 1% based on annual net revenues, as defined in the Revenue Interest Agreement (or 14% to 1.5% if the Third Investment Amount is funded). The applicable royalty rate is subject to a one-time step-down if certain sales milestones are met. When HCR has received aggregate payments equal to the 250% of the Investment Amount (the "Hard Cap"), HCR's right to receive royalties on net revenues will terminate.

If we have not received FDA approval for tebipenem HBr for a cUTI indication on or prior to December 31, 2022, the Revenue Interest Agreement will terminate and we must pay to HCR an amount equal to the initial investment amount of $50.0 million plus interest equal to a 13.5% annual rate of return. If HCR has not received aggregate payments of at least 60% of the amount funded by HCR to date by September 30, 2025 and at least 100% of the amount funded by HCR to date by September 30, 2027, then we must make a cash payment within 45 calendar days of the applicable date to HCR in an amount sufficient to gross HCR up to such minimum amounts after giving full consideration of the cumulative amount we paid to HCR through each date.

When HCR has received aggregate payments equal to the Hard Cap, HCR's right to receive royalties on net revenues will terminate. If an event of default or a change of control of us occurs, we must immediately repay HCR an amount equal to the Hard

Cap, minus aggregate payments made to HCR under the Revenue Interest Agreement, and the Revenue Interest Agreement will terminate. In the event of certain other material breaches of the Revenue Interest Agreement or the occurrence of a "material adverse effect" (as defined therein), HCR will have the right to terminate the Revenue Interest Agreement, whereby we must pay to HCR an amount equal to the initial investment amount, plus a 15% annual rate of return, minus aggregate payments made to HCR under the Revenue Interest Agreement. In the event that the Revenue Interest Agreement terminates on the twelfth anniversary of the initial closing, we may be required to make a payment to HCR at that time to ensure that HCR will have received aggregate payments equal to the total investment amount funded, plus a 2% annual rate of return over the term of the Revenue Interest Agreement.

Pursuant to the Revenue Interest Agreement, we agreed to specified affirmative and negative covenants, including covenants to use commercially reasonable efforts to promote tebipenem HBr in the United States; prosecute and defend intellectual property rights; periodic reporting of information by us to HCR; audits of royalty payments made under the Revenue Interest Agreement; and restrictions on the ability of us or any of our subsidiaries to incur indebtedness, subject to certain exceptions. The Revenue Interest Agreement also contains representations and warranties, other covenants, indemnification obligations, and other provisions customary for transactions of this nature.

In connection with the Revenue Interest Agreement, we also entered into a Security Agreement with HCR's collateral agent, pursuant to which we granted HCR a first-priority blanket lien on tebipenem HBr assets, including tebipenem HBr patent rights, tebipenem HBr regulatory approvals, and tebipenem HBr material contracts, as well as future cash receipts relating to product sales. Additionally, we will grant HCR a lien on equity interests of any subsidiaries that hold tebipenem HBr-related assets and any such subsidiaries will become guarantors under the Security Agreement. In the event of an event of default under the Revenue Interest Agreement, HCR would have the right to foreclose on the pledged collateral and exercise customary creditors' rights and remedies under a deposit account control agreement covering a collection account that will receive all revenues from product sales.

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

We have not generated any revenue from the sale of our products and have incurred losses in each year since our inception in 2013. Our net losses were $32.8 million and $19.4 million during the three months ended March 31, 2022 and 2021, respectively. All of our product candidates are in development, none have been approved for sale and we may never have a product candidate approved for commercialization.

In accordance with ASU 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40), we are required to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern from the issuance date of our financial statements. Based on our recently announced restructuring and the cessation of commercialization activities for the tebipenem HBr program and assuming the repayment of amounts under our Revenue Interest Agreement, we believe that our existing cash, cash equivalents and marketable securities, together with other non-dilutive funding commitments, will be sufficient to fund our planned operating expenses and capital expenditures pursuant to the priorities of our strategic refocusing through late 2023. This timeline is subject to uncertainty as to the timing of future expenditures. We have developed plans to mitigate this risk, which primarily consist of raising additional capital through some combination of equity or debt financings, potential new collaborations or partnerships, additional grant funding and/or reducing cash expenditures. If we are not able to secure adequate additional funding, we plan to make reductions in spending. In that event, we may have to delay, scale back, or eliminate some or all of our planned clinical trials, research stage programs and commercial activities. The actions necessary to reduce spending under this plan at a level that mitigates the factors described above is not considered probable, as defined in the accounting standards and therefore, the full extent to which management may extend our funds through these actions may not be considered in management's assessment of our ability to continue as a going concern. As a result, we have concluded that substantial doubt exists about our ability to continue as a going concern.

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

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

- conduct additional clinical trials and studies of our product candidates;
- continue to discover and develop additional product candidates;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of any product candidates for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, scientific and commercial personnel;

- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, face competing technological and market developments; and
- acquire or in-license other product candidates and technologies.

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.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete. We expect that our expenses will continue to increase as we commence and advance our ongoing and planned clinical trials and other studies of SPR720 and SPR206. If we obtain marketing approval for any 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.

Based on our recently announced restructuring and the cessation of commercialization activities for the tebipenem HBr program and assuming the repayment of amounts under our Revenue Interest Agreement, we believe that our existing cash, cash equivalents and marketable securities, together with other non-dilutive funding commitments, will be sufficient to fund our planned operating expenses and capital expenditures pursuant to the priorities of our strategic refocusing through late 2023. 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:

- whether the FDA determines that our Phase 3 ADAPT-PO trial of tebipenem HBr in the treatment of patients with cUTI, including AP, is or is not sufficient for regulatory approval to treat cUTI, including pyelonephritis;
- the timing, costs and results of our ongoing, planned and potential clinical trials for our product candidates;
- the amount of funding that we receive under our government awards;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for our product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the terms and timing of any future collaborations, licensing or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to our license agreements;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;
- the costs of our continued operation as a public company; and
- the extent to which we in-license or acquire other products and technologies.

As of March 31, 2022, our non-dilutive sources of funding consisted of an award from BARDA for tebipenem HBr, an award from NIAID under its Small Business Innovation Research program ("SBIR") for our SPR720 program, an award from NIAID for SPR206, an award from the DoD that provides partial funding for the development of SPR206 and an award from the DoD Congressionally Directed Medical Research Programs ("CDMRP") Joint Warfighter Medical Research Program for SPR206.

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

Unless and until we can generate a substantial amount of revenue from our product candidates, we expect to finance our future cash needs through public or private equity offerings, debt financings, collaborations, licensing arrangements and government funding arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. We filed a universal shelf registration statement on Form S-3 (Registration No. 333-254170) with the SEC on March 11, 2021, which was declared effective on March 29, 2021 and pursuant to which we registered for sale up to $300.0 million of any combination of our common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that we may determine, including up to $75.0 million of our common stock available for issuance pursuant to an “at-the-market” offering program sales agreement that we entered into with Cantor. Under the sales agreement, Cantor may sell shares of our common stock by any method permitted by law deemed to be an “at the market” offering as defined in Rule 415 of the Securities Act, 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, 2021, we had United States federal, state and foreign net operating loss carryforwards ("NOLs") of $303.7 million, $302.6 million and $4.4 million, respectively. The federal NOLs of $73.0 million will expire at various dates from 2033 to 2037 and approximately $230.7 million can be carried forward indefinitely. The state NOLs begin to expire in 2033 and will expire at various dates through 2039. The foreign NOLs do not expire. Utilization of these NOLs depends on many factors, including our future income, which cannot be assured. These NOLs could expire unused and be unavailable to offset our future income tax liabilities. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended (the "Code") and corresponding provisions of state law, if a corporation undergoes an “ownership change,” which is generally defined as a greater than 50% change, by value, in its equity ownership by 5% stockholders over a three-year period, the corporation’s ability to use its pre-change NOLs and other pre-change tax attributes to offset its post-change income may be limited. We have not determined if we have experienced Section 382 ownership changes in the past and if a portion of our NOLs is subject to an annual limitation under Section 382. In addition, we may experience ownership changes in the future as a result of subsequent changes in our stock ownership, some of which may be outside of our control. If we determine that an ownership change has occurred and our ability to use our historical NOLs is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

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

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

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

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We have begun 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 the COVID-19 Pandemic

The continued COVID-19 pandemic could adversely impact our business, including our preclinical studies and clinical trials.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. In December 2019, a novel strain of coronavirus, SARS-CoV-2, which causes coronavirus disease 2019 ("COVID-19"), surfaced in Wuhan, China. Since then, COVID-19 and variants thereof have spread globally.

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

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

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

The COVID-19 outbreak continues to evolve rapidly. The extent to which the outbreak may impact our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the outbreak, travel restrictions and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

Risks Related to Our 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.

We may seek third-party collaborators for development and commercialization of certain of our product candidates. Currently we are party to license and collaboration agreements with third parties as described in Note 9 ("License Collaborations and Services Agreements") to the audited financial statements filed herewith. 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 our product candidates. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. Moreover, we intend to utilize a variety of types of collaboration arrangements for the potential commercialization of our product candidates outside the United States. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include:

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

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

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

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

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

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

participating in clinical trials. The FDA enforces these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable GCP standards, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the regulatory approval process. We cannot make assurances that, upon inspection, the FDA will determine that any of our clinical trials comply with GCP. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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

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

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

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

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

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

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

Our third-party contract manufacturers are based in Asia. Recently, our third-party contract manufacturers have been subject to various supply chain disruptions. These supply chain disruptions have increased the price of certain materials due to the significant

increase in costs of raw materials and shipping costs. Our ability to produce and timely deliver our products may be materially impacted in the future if these supply chain disruptions continue or worsen.

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

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

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

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

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

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

For example, we have an exclusive know-how license with Meiji (the "Meiji License") that gives us rights outside of specified countries in Asia to develop, manufacture, and commercialize tebipenem HBr as well as the right to use, cross-reference, file or incorporate by reference any information and relevant Meiji regulatory documentation to support any regulatory filings outside of Asia. In addition, we have the right to develop, manufacture and have manufactured tebipenem HBr in Asia solely for the purpose of furthering development, manufacturing and commercialization of tebipenem HBr outside of Asia. In exchange for those rights, we are obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop and commercialize tebipenem HBr and to implement a specified development plan, meeting specified development milestones and providing an update on progress on an annual basis. The Meiji License requires us to pay future milestone payments of up to $1.0 million upon the achievement of specified clinical and regulatory milestones and royalties of a low single-digit percentage on net sales on a country-by-country basis.

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

Risks Related to Our United States Government Contracts and to Certain Grant Agreements

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

- the Federal Acquisition Regulations (the "FAR") and agency-specific regulations supplemental to the FAR, which comprehensively regulate the procurement, formation, administration and performance of government contracts;
- business ethics and public integrity obligations, which govern conflicts of interest and the hiring of former government employees, restrict the granting of gratuities and funding of lobbying activities and include other requirements such as the Anti-Kickback Statute and the Foreign Corrupt Practices Act;
- export and import control laws and regulations; and

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

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

Provisions in our United States government contracts, including our contracts with BARDA, may affect our intellectual property rights.

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

Risks Related to Our Intellectual Property

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

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

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

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

The laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, in the US there is an exception for one's own publication of an invention prior to filing a patent application for the invention. Most other countries have no such exception and any publication prior to filing is an absolute bar to patentability. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result of the America Invents Act of 2011, the United States transitioned to a first-inventor-to-file system in March 2013, under which, assuming the other requirements for patentability are met, the first inventor to file a patent application is entitled to the patent. However, as a result of the lag in the publication of patent applications following filing in the United States, we are still not be able to be certain upon filing that we are the first to file for patent protection for any invention. Moreover, we may be subject to a third-party preissuance submission of prior art to the USPTO or become involved in opposition, derivation, reexamination, *inter partes* review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

We have registered our trademarks for our name and logo in the United States and other countries and have a number of pending trademark applications in the United States and other countries. As of March 31, 2022, we have two registered United States trademarks, 21 registered foreign trademarks, and four pending foreign trademark applications. If our registered trademarks are invalidated, we may be unable to exclusively use our name or logo in certain jurisdictions or may need to change our name or logo in certain jurisdictions, which could affect our business. If we do not secure registrations for our pending trademark applications, we may encounter more difficulty in enforcing them against third parties, which could adversely affect our business.

We have applied to register our product candidate name as a trademark in the United States, where it has been allowed for registration, and have applied to register the mark in three foreign jurisdictions. We have also applied to register additional product candidate names as trademarks in the United States. When we file trademark applications for our product candidates, those applications may not be allowed for registration, and registered trademarks may not be obtained, maintained, or enforced. During trademark registration proceedings in the United States and foreign jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but we may not be able to overcome such rejections. In addition, in the United States Patent and Trademark Office and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings.

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

Risks Related to Regulatory Approval and Other Legal Compliance Matters

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

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable foreign regulatory authorities, with regulations differing from country to country. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate.

We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and have relied on third-party contract research organizations to assist us in this process.

The time required to obtain approval, if any, by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate’s clinical development and may vary among jurisdictions. We have not

obtained regulatory approval for any product candidate and it is possible that neither tebipenem HBr nor any product candidates we may seek to develop in the future will ever obtain regulatory approval. Neither we nor any future collaborators are permitted to market any of our product candidates in the United States until we or they receive regulatory approval of an NDA from the FDA.

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

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

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

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

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

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

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

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

If the FDA determines that a product candidate intended to treat a serious disease, if approved, would provide a significant improvement in safety or effectiveness of the treatment of the disease, the FDA may designate the drug application for that product candidate for priority review. A priority review designation means that the goal for the FDA to review the marketing application is six months from the date of NDA acceptance for filing, rather than the standard review period of ten months from the date of NDA acceptance for filing. In January 2022, FDA accepted our NDA for tebipenem HBr and granted it a priority review designation, with a June 27, 2022 target action date. A priority review designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving a priority review designation from the FDA does not guarantee approval of the drug application within the six-month review cycle or any time thereafter. For example, in May 2022, we announced that we are suspending current commercialization activities for tebipenem HBr based on feedback from our LCM with the FDA, and although the review is still ongoing and the FDA has not yet made any final determination regarding approvability, the discussion suggested that the data package may be insufficient to support approval during this review cycle.

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

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

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

Even though we have obtained orphan drug designation for SPR720 and may seek orphan drug designation for other product candidates in the future, there is no assurance that we will be the first to obtain marketing approval for NTM infection or for any particular rare indication. Further, even though we have obtained orphan drug designation for SPR720, or even if we obtain orphan drug designation for other product candidates, such designation may not effectively protect us from competition because different drugs can be approved for the same condition and the same drug can be approved for different conditions and potentially used off-label in the orphan indication. Even after an orphan drug is approved, the FDA can subsequently approve a competing drug for the same condition for several reasons, including, if the FDA concludes that the later drug is safer or more effective or makes a major

contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

If approved for commercial marketing in the United States, our product candidates may face generic competition sooner than anticipated.

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

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

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

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

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

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

In addition, even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed, may be subject to significant conditions of approval or may impose requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA may also require a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and

other risk minimization tools. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure that drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling and regulatory requirements. The FDA also imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not restrict the marketing of our products only to their approved indications, we may be subject to enforcement action for off-label marketing.

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

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

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

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

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

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

violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

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

We will be required to spend substantial time and money to ensure that our business arrangements with third parties, and our business generally, comply with applicable healthcare laws and regulations. Even then, governmental authorities may conclude that our business practices, including arrangements we may have with physicians and other healthcare providers, do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If governmental authorities find that our operations violate any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, imprisonment, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and we may be required to curtail or restructure our operations. Moreover, we expect that there will continue to be federal and state laws and regulations, proposed and implemented, that could affect our operations and business. For example, in November 2020, DHHS finalized significant changes to the regulations implementing the Anti-Kickback Statute, as well as the civil monetary penalty rules regarding beneficiary inducements, with the goal of offering the healthcare industry more flexibility and reducing the regulatory burden associated with those fraud and abuse laws, particularly with respect to value-based arrangements among industry participants. The extent to which future legislation or regulations, if any, relating to healthcare fraud and abuse laws or enforcement, may be enacted or what effect such legislation or regulation would have on our business remains uncertain.

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

The pricing and reimbursement environment may become more challenging due to, among other reasons, policies advanced by the presidential administration, federal agencies, new healthcare legislation passed by the United States Congress or fiscal challenges faced by all levels of government health administration authorities. Among policy makers and payors in the United States and foreign countries, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in

connection with the sale of any products for which we obtain marketing approval, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals. Resulting legislative, administrative, or policy changes from payors may reduce payments for any products for which we obtain marketing approval and could affect future revenues.

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

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and as a result certain sections of the ACA have not been fully implemented or effectively repealed. However, following several years of litigation in the federal courts, in June 2021, the U.S. Supreme Court upheld the ACA when it dismissed a legal challenge to the ACA's constitutionality. Further legislative and regulatory changes under the ACA remain possible, although the new federal administration under President Biden has signaled that it plans to build on the ACA and expand the number of people who are eligible for health insurance subsidies under it. It is unknown what form any such changes or any law would take, and how or whether it may affect the pharmaceutical industry as a whole or our business in the future. We expect that changes or additions to the ACA, the Medicare and Medicaid programs, such as changes allowing the federal government to directly negotiate drug prices, and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry in the United States.

Beginning on April 1, 2013, Medicare payments for all items and services under Part A and B, including drugs and biologicals, and most payments to plans under Medicare Part D were reduced by 2%, or automatic spending reductions, required by the Budget Control Act of 2011 ("BCA"), as amended by the American Taxpayer Relief Act of 2012. The BCA requires sequestration for most federal programs, excluding Medicaid, Social Security, and certain other programs. The BCA caps the cuts to Medicare payments for items and services and payments to Part D plans at 2%. As long as these cuts remain in effect, they could adversely affect payment for our product candidates, if approved for commercial marketing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures. The Coronavirus Aid, Relief, and Economic Security Act (the "CARES Act"), which was signed into law on March 27, 2020 and was designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2030, in order to offset the added expense of the 2020 cancellation. The suspension was subsequently extended through March 31, 2022, with a reduction of the suspension to 1% sequester through June 30, 2022.

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. There have been several United States Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers ("PBMs") and other members of the health care and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the effect of such changes on the marketing approvals of our product candidates, if any, may be. As another example, in 2020, the FDA finalized a rulemaking to establish a system whereby state governmental entities could lawfully import and distribute prescription drugs sourced from Canada. More recently, in July 2021, President Biden issued a sweeping executive order on promoting competition in the American economy that includes several mandates pertaining to the pharmaceutical and healthcare insurance industries. Among other things, the executive order directed the FDA to work towards implementing a system for importing drugs from Canada (following on the Trump administration notice-and-comment rulemaking on Canadian drug importation that was finalized in October 2020). The Biden order also called on DHHS to

release a comprehensive plan to combat high prescription drug prices, and it includes several directives regarding the Federal Trade Commission's oversight of potentially anticompetitive practices within the pharmaceutical industry. The drug pricing plan released by DHHS in September 2021 in response to the executive order makes clear that the Biden Administration supports aggressive action to address rising drug prices, including allowing DHHS to negotiate the cost of Medicare Part B and D drugs, but such significant changes will require either new legislation to be passed by Congress or time-consuming administrative actions. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. We expect that additional state and federal health care reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for health care products and services.

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

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

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

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

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

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

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC

and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

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

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.

On May 3, 2022, we implemented a restructuring that reduced our workforce from 146 full-time employees as of December 31, 2021 to approximately 35 full-time employees. Pursuant to the restructuring and effective as of July 2, 2022, Cristina Larkin will separate from us as our Chief Operating Officer and David Melnick, M.D. will separate from us as our Chief Medical Officer. While we have confidence in our remaining leadership team, including the board of directors, the uncertainty inherent in this ongoing restructuring may be difficult to manage, may cause concerns from third parties with whom we do business, and may increase the likelihood of turnover of other key officers and employees.

If we lose one or more of our other 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 are undertaking internal restructuring activities that could result in disruptions to our business or otherwise materially harm our results of operations or financial condition.

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

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

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

- potentially reduced protection for intellectual property rights;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;

- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting a product candidate and/or finished drug product supply or manufacturing capabilities abroad;
- business interruptions resulting from geo-political actions, including war and terrorism, health epidemics or natural disasters, including earthquakes, hurricanes, typhoons, floods and fires; and
- failure to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act.

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

Risks Related to Our Common Stock

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

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

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

In addition, the stock market has experienced significant volatility, particularly with respect to pharmaceutical, biotechnology and other life sciences company stocks. The volatility of pharmaceutical, biotechnology and other life sciences company stocks often does not relate to the operating performance of the companies represented by the stock. In the past, securities class action litigation has

often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources, and could also require us to make substantial payments to satisfy judgments or to settle litigation.

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

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

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

Our amended and restated certificate of incorporation, as amended, 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 ("Series A Preferred Stock") to certain affiliates of Biotechnology Value Fund, L.P. ("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 ("Series B Preferred Stock"), each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. In June 2019, BVF converted 500 shares of Series A Preferred Stock into 500,000 shares of our common stock pursuant to BVF's rights under the certificate of designation for such Series A Preferred Stock. In December 2020, BVF converted the remaining 1,720 shares of Series A Preferred Stock into 1,720,000 shares of our common stock pursuant to BVF's rights under the certificate of designation for such Series A Preferred Stock. In addition, in February 2021, BVF converted 62 shares of Series B Preferred Stock into 62,000 shares of our common stock pursuant to BVF's rights under the certificate of designation for such Series B Preferred Stock. In connection with our rights offering, which we launched in February 2020 and closed in early March 2020, we issued 2,287 shares of our Series C Convertible Preferred Stock ("Series C Preferred Stock") to BVF. In February 2021, BVF converted 73 shares of Series C Preferred Stock into 73,000 shares of our common stock, pursuant to BVF's rights under the certificate of designation for such Series C Preferred Stock. In September 2020, in connection with our underwritten public offering, we issued 3,215,000 shares of our Series D Convertible Preferred Stock to BVF. If BVF or any other future holders of our shares of preferred stock convert their shares into common stock, existing holders of our common stock will experience dilution.

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

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

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"), and may remain an emerging growth company for up to five years. We would cease to be an emerging growth company upon the earlier of: (i) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of our initial public offering, which is December 31, 2022; (iii) the

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

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

We are subject to Section 404 of The Sarbanes-Oxley Act of 2002 ("Section 404") and the related rules of the SEC, which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. However, for so long as we remain an emerging growth company as defined in the JOBS Act, or a "smaller reporting company" ("SRC") and non-accelerated filer, we intend to take advantage of certain exemptions from various reporting requirements, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404. Once we are no longer an emerging growth company and otherwise do not meet the definition of a SRC and non-accelerated filer or, if prior to such date, we opt to no longer take advantage of the applicable exemption, we will be required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal controls over financial reporting. We could qualify as a SRC if the market value of our common stock held by non-affiliates is below $250.0 million (or $700.0 million if our annual revenue is less than $100.0 million) as of June 30 in any given year.

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

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

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

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

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Our outstanding shares of common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act of 1933, as amended (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, 2022, 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 46% 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, as amended, and amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that our stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

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

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

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

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

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

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

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

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

None.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures.

Not Applicable.

Item 5. Other Information.

None.

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*	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, by Principal Executive Officer and Principal Financial Officer	X			
101.INS	XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document	X			
101.SCH	Inline XBRL Taxonomy Extension Schema Document	X			
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X			
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	X			
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	X			

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

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 16, 2022

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

Date: May 16, 2022

By: /s/ Satyavrat Shukla
Satyavrat Shukla
Chief Financial Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer)

Exhibit 31.1

CERTIFICATIONS UNDER SECTION 302

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 control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

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

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

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

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

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

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

Date: May 16, 2022

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

Exhibit 31.2

CERTIFICATIONS UNDER SECTION 302

I, Satyavrat Shukla, certify that:

1. I have reviewed this 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 control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

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

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

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

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

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

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

Date: May 16, 2022

/s/ Satyavrat Shukla
Satyavrat Shukla
Chief Financial Officer and Treasurer
(Principal Financial Officer)

Exhibit 32

CERTIFICATIONS UNDER SECTION 906

Pursuant to section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), each of the undersigned officers of Spero Therapeutics, Inc., a Delaware corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Quarterly Report for the quarter ended March 31, 2022 (the "Form 10-Q") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-Q fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: May 16, 2022

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

Dated: May 16, 2022

/s/ Satyavrat Shukla
Satyavrat Shukla
Chief Financial Officer and Treasurer
(Principal Financial Officer)