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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 16, 2022

SPERO THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-38266**	**46-4590683**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

675 Massachusetts Avenue, 14th Floor Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	**(Zip Code)**

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

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c)

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 is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

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. ☒

Item 2.02. Results of Operations and Financial Condition.

On May 16, 2022, Spero Therapeutics, Inc. (the "Company") issued a press release announcing its results for the quarter ended March 31, 2022. A copy of the press release is furnished as Exhibit 99.1 hereto.

The information contained in this Item 2.02 and in the press release furnished as Exhibit 99.1 hereto shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that Section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended, or incorporated by reference in any filing with the U.S. Securities and Exchange Commission made by the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1	Press Release, dated May 16, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

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 hereunto duly authorized.

SPERO THERAPEUTICS, INC.

Date: May 16, 2022

By: /s/ Tamara Joseph
Tamara Joseph
Chief Legal Officer

Exhibit 99.1

Spero Therapeutics Announces First Quarter 2022 Operating Results and Provides Business Update

New Strategic Direction Focuses on Advancing the Clinical Stage Pipeline and Identifying Tebipenem's Optimal Path to Value Creation

Initiation of a Phase 2 Trial of SPR720 in Nontuberculous Mycobacterial-Pulmonary Disease Expected in 2H 2022

SPR206's Phase 1 Data Support Further Development in Complicated Urinary Tract Infection, Hospital-acquired and Ventilator-associated Bacterial Pneumonia, and Bloodstream Infections

Conference Call and Live Webcast at 4:30 p.m. ET Today

CAMBRIDGE, Mass., May 16, 2022 — Spero Therapeutics, Inc. (Nasdaq: SPRO) today announced financial results for the first quarter ended March 31, 2022 and provided a business update.

"While our recent decision to restructure the company's operations was immensely difficult, we remain optimistic about our future outlook," said Ankit Mahadevia, M.D., Chief Executive Officer of Spero Therapeutics. "Our plan for Spero going forward is to focus on delivery of key clinical and regulatory milestones, clarify and execute the path forward for tebipenem, and do so while being good stewards of capital and continuing to pursue creative partnerships. Both SPR720 and SPR206 seek to address pressing unmet needs for patients with serious drug-resistant infections and are supported by robust clinical and preclinical datasets that we believe clearly differentiate them from competing approaches. We expect their advancement into Phase 2 trials in NTM-pulmonary disease and multi-drug resistant Gram-negative infections, respectively, will provide us with a steady cadence of value inflection points moving forward."

Dr. Mahadevia continued, "We also believe tebipenem HBr has the potential to deliver substantial clinical value to healthcare providers, payers, and patients, if approved. We are pleased to maintain stewardship of the asset and are committed to pursuing a potential path forward to regulatory approval, either independently or with a partner. As we look ahead, we believe the diverse nature of our multi-asset pipeline, together with cash runway through late 2023, leaves us positioned to execute on our strategic objectives."

Program Highlights and Upcoming Milestones

SPR720:

- On January 4, 2022, Spero announced that the United States Food and Drug Administration (FDA) had lifted the clinical hold previously placed on the Phase 2 trial of SPR720, Spero's investigational oral product candidate being developed for nontuberculous mycobacterial (NTM) disease. Subsequently, in the first quarter of 2022, Spero engaged with the FDA to discuss the re-initiation and planned protocol and trial design of the SPR720 Phase 2 trial in NTM-pulmonary disease (NTM-PD) patients. Spero continues to engage with the FDA on specifics of the upcoming trial and expects to begin this study in the second half of 2022, with an expected interim data read-out in 2023 and topline results in 2024.

SPR206:

- A Pre-IND Meeting for SPR206 has been scheduled for the second quarter of 2022, with expectations for a Phase 2, cross-indication resistant pathogen study to begin in the second quarter of 2023. SPR206 will be evaluated in patients with complicated urinary tract infection (cUTI), hospital-acquired and ventilator-associated bacterial pneumonia (HABP/VABP) and bloodstream infections (BSI).
- In February 2022, Spero announced topline results from a Phase 1 bronchoalveolar lavage (BAL) trial of SPR206, the company's novel intravenous (IV)-administered next generation polymyxin antibiotic being developed to treat multi-drug resistant (MDR) Gram-negative bacterial infections. These results showed that SPR206 was generally well tolerated and achieved mean lung epithelial lining fluid exposures above its MIC (minimum inhibitory concentration) for targeted gram-negative pathogens for the entirety of its eight-hour dosing period when administered three times daily at 100 mg. These data are consistent with prior Phase 1 results showing SPR206's lack of nephrotoxicity at predicted therapeutic dose levels.
- The Phase 1 renal impairment trial for SPR206 has been completed, annotating final safety and pharmacokinetic (PK) data, providing data-driven guidance on how to adjust for renally impaired patients in future clinical trials.
- Funding for the SPR206 BAL and renal impairment clinical trials was provided by the United States Department of Defense (DoD) under Award Number W81XWH-1910295. The SPR206 program is also supported by funding from the National Institute of Allergy and Infectious Diseases (NIAID) and is the subject of a license agreement with Pfizer Inc., which was entered into alongside Pfizer's previously announced $40 million equity investment in Spero. Pursuant to the licensing agreement between the parties, Spero granted Pfizer the rights to develop, manufacture, and commercialize SPR206 in ex-U.S. and ex-Asia territories. In exchange for these rights, Spero is eligible to receive up to $80 million in development and sales milestones, and high single digit to low double-digit royalties on net sales of SPR206 in these territories.

Tebipenem HBr:

- On January 3, 2022, Spero announced that the FDA had accepted for filing its New Drug Application (NDA) seeking approval for tebipenem HBr oral tablets for treatment in adult patients with certain bacterial microorganisms that cause cUTI, including pyelonephritis, for substantive review. The NDA was granted Priority Review designation and a Prescription Drug User Fee Act (PDUFA) goal action date was set for June 27, 2022. In late March 2022, the FDA notified Spero that, during its ongoing review of the NDA for tebipenem HBr, it had identified deficiencies that precluded discussion of labeling and post-marketing requirements/commitments at that time. Based on feedback from a Late Cycle Meeting (LCM) with the FDA in April, Spero made the decision to immediately suspend current commercialization activities for tebipenem HBr. Although the NDA review is still ongoing and the FDA has not yet made any final determination regarding approvability, discussions

during the LCM suggested that the data package may be insufficient to support approval during this review cycle. Spero is continuing its dialogue with the FDA, as the company seeks a pathway forward for potential approval of tebipenem HBr in order to enable eventual commercialization by Spero or commercialization through partnership.

- In April 2022, results from the Phase 3 ADAPT-PO trial of tebipenem HBr were published in ***The New England Journal of Medicine***. ADAPT-PO was a global, randomized, placebo-controlled clinical trial that evaluated the safety and efficacy of oral tebipenem HBr versus IV ertapenem for the treatment of adults with cUTI, including acute pyelonephritis.
- In January 2022, Spero was awarded up to an additional $12.9 million by the Biomedical Advanced Research and Development Authority (BARDA) to support the development of orally administered tebipenem pivoxil in pediatric patients. This additional funding was granted via a new option to a contract originally awarded to Spero in 2018, bringing the total potential value of the contract up to $59.7 million. The additional $12.9 million option would be available to provide support for a clinical trial and related activities designed to advance orally administered tebipenem HBr development as a treatment for pediatric patients with cUTI, including acute pyelonephritis.

Medical Congress Engagement

- In April 2022, scientific information regarding tebipenem HBr was featured in two oral and four poster presentations at the 32nd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). The oral presentations included discussions of the plasma pharmacokinetics and intrapulmonary penetration of tebipenem HBr in healthy subjects, as well as tebipenem HBr's effects on the normal gut microbiota of healthy adults. The four posters presented additional data related to tebipenem HBr, including Spero's poster P0213, which was selected by the ECCMID Program Committee as one of the top-rated posters for this year's Congress.

First Quarter 2022 Financial Results

Spero reported a net loss for the first quarter ended March 31, 2022 of $32.8 million or $1.01 per common share, compared to a net loss of $19.4 million or $0.66 per common share reported for the same period in 2021.

Total revenues for the first quarter of 2022 were $2.1 million, compared with revenues of $7.3 million in the first quarter of 2021. The revenue decrease was primarily due to a decrease in qualified expenses incurred under the BARDA contract for tebipenem HBr, a decrease in funding under the NIAID agreement related to SPR206, partially offset by an increase under the DOD agreement relating to SPR206, and an increase in collaboration revenues related to the Pfizer agreement.

Research and development expenses for the first quarter of 2022 were $17.0 million, compared with $18.4 million, of research and development expenses for the same period in 2021. This year-over-year decrease was primarily due to the completion of significant activities to support the NDA for tebipenem HBr, the Phase 2 clinical hold for SPR720, offset by direct costs related to the SPR206 program, and increase in personnel related costs.

General and administrative expenses for the first quarter of 2022 of $15.3 million were higher than the $8.3 million reported in the same period in 2021, primarily due to an increase in headcount in our commercial, general and administrative functions.

As of March 31, 2022, Spero had cash, cash equivalents, and marketable securities of $122 million. Based on the previously announced restructuring and the cessation of commercialization activities for the tebipenem HBr program and assuming the repayment of amounts under the company's Revenue Interest Financing Agreement with certain entities managed by HealthCare Royalty Management, LLC, Spero believes that its existing cash, cash equivalents and marketable securities, together with other non-dilutive funding commitments, will be sufficient to fund its planned operating expenses and capital expenditures pursuant to the priorities of its strategic refocusing through late 2023. During this period, the strategic refocusing prioritizes advancing SPR720 and SPR206 to key Phase 2 milestones.

Conference Call and Webcast

Spero will host a conference call and webcast today at 4:30 p.m. ET. To access the call, please dial 1-877-704-4453 (domestic) or 1-201-389-0920 (international) and refer to conference ID 13729221. The conference call will also be webcast live and a link to the webcast can be accessed here and on Spero Therapeutics' website at ***www.sperotherapeutics.com*** in the "Investors and Media" section under "Events and Presentations." An archived webcast will be available on Spero's website for 30 days following the presentation.

Tebipenem HBr Research Support

Select tebipenem HBr studies have been funded in part with federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, under contract number HHSO100201800015C.

Government Agency Research Support

The views expressed in this press release are those of the authors and may not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government.

Department of Defense

Select SPR206 studies are supported by the Office of the Assistant Secretary of Defense for Health Affairs, through the Joint Warfighter Medical Research Program under Award No. W81XWH 19 1 0295. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Department of Defense.

National Institute of Allergy and Infectious Disease

Select SPR206 studies have been funded in whole or in part with Federal funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under Contract No. 75N93021C00022.

About Spero Therapeutics

Spero Therapeutics is a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing, and commercializing novel treatments for bacterial infections, including multi-drug resistant bacterial infections and rare diseases.

- The NDA for tebipenem pivoxil oral tablets (tebipenem HBr) is currently being reviewed by the FDA; tebipenem HBr is not FDA-approved.
- Tebipenem HBr is an investigational drug in the United States being developed for the treatment of cUTI, including pyelonephritis, caused by certain microorganisms, in adult patients who have limited oral treatment options.
- Spero Therapeutics is developing SPR720 as a novel oral therapy candidate for the treatment of a rare, orphan pulmonary disease caused by non-tuberculous mycobacterial infections.
- Spero Therapeutics also has an IV-administered next generation polymyxin product candidate, SPR206, developed from its potentiator platform, which is in development to treat multi-drug resistant Gram-negative infections in the hospital setting.

For more information, visit ***https://sperotherapeutics.com***.

Forward Looking Statements

This press release may contain forward-looking statements. These statements include, but are not limited to, statements about the potential regulatory path forward for tebipenem HBr and the potential approval of tebipenem HBr by the FDA and the timing thereof; the potential value of tebipenem HBr; the potential for a partnership of the tebipenem HBr franchise; the future development and commercialization of SPR206 and SPR720; the design, initiation, timing, progress and results of Spero's preclinical studies and clinical trials and its research and development programs; management's assessment of the results of such preclinical studies and clinical trials; and the expected cost-savings from the restructuring, Spero's anticipated expenses and its anticipated cash runway. In some cases, forward-looking statements can be identified by terms such as "may," "will," "should," "expect," "plan," "aim," "anticipate," "could," "intent," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including whether the FDA will ultimately approve tebipenem HBr and, if so, the timing of any such approval; whether the FDA will require any additional clinical data or place labeling restrictions on the use of tebipenem HBr that would add costs for Spero, delay approval and/or reduce the commercial prospects of tebipenem HBr; whether any third parties would be interested in partnering with Spero to pursue continued efforts to obtain FDA approval of tebipenem HBr, or acquiring rights to the tebipenem HBr program from Spero through a partnership arrangement; the COVID-19 pandemic; Spero's need for additional funding; Spero's ability to successfully implement the restructuring; the impact of the restructuring on Spero's business, including estimated costs related thereto; the risk that Spero may not be able to address the FDA's concerns with respect to tebipenem HBr; the lengthy, expensive, and uncertain process of clinical drug development for SPR720 and SPR206; whether results obtained in preclinical studies and clinical trials will be indicative of results obtained in future clinical trials; Spero's reliance on third parties

to manufacture, develop, and commercialize its product candidates, if approved; the ability to commercialize Spero's product candidates, if approved; Spero's ability to retain key personnel; whether Spero's cash resources will be sufficient to fund its continuing operations for the periods and/or trials anticipated; and other factors discussed in the "Risk Factors" set forth in filings that Spero periodically makes with the U.S. Securities and Exchange Commission. The forward-looking statements included in this press release represent Spero's views as of the date of this press release. Spero anticipates that subsequent events and developments will cause its views to change. However, while Spero may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Spero's views as of any date subsequent to the date of this press release.

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Spero Therapeutics, Inc.
Condensed Consolidated Statements of Operations
(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)	(2,622)	(20)
Net loss	$ (32,829)	$ (19,423)
Net loss attributable to common shareholders of Spero Therapeutics, Inc.	$ (32,829)	$ (19,423)
Net loss per share attributable to common shareholders per share, basic and diluted	$ (1.01)	$ (0.66)
Weighted average shares outstanding, basic and diluted:	32,606,715	29,414,148

Spero Therapeutics, Inc.
Condensed Consolidated Balance Sheet Data
(in thousands)
(Unaudited)

	March 31, 2022	December 31, 2021
Cash, cash equivalents and marketable securities	$121,966	$ 146,402
Other assets	23,864	24,670
Total assets	**$145,830**	**$ 171,072**
Total liabilities	83,357	82,783
Total stockholder's equity	62,473	88,289
Total liabilities and stockholders' equity	**$145,830**	**$ 171,072**