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): March 11, 2021

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 March 11, 2021, Spero Therapeutics, Inc. (the "Company") issued a press release announcing its results for the fourth quarter and full year ended December 31, 2020. 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 March 11, 2021
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: March 11, 2021

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

Exhibit 99.1

Spero Therapeutics Announces Fourth Quarter and Full-Year 2020 Operating Results and Provides Business Update

Tebipenem HBr advancing towards NDA submission in the second half of 2021

Conference call and live webcast at 4:30 p.m. EST today

CAMBRIDGE, Mass., March 11, 2021 — Spero Therapeutics, Inc. (Nasdaq: SPRO), a multi-asset clinical-stage biopharmaceutical company focused on identifying, developing and commercializing treatments in high unmet need areas involving multi-drug resistant bacterial infections and rare diseases, today announced financial results for the fourth quarter and full-year ended December 31, 2020 and provided a business update.

“Over the last year we have made significant progress and completed critical milestones despite the industry-wide challenges brought about by the COVID-19 pandemic,” said Ankit Mahadevia, M.D., Chief Executive Officer of Spero Therapeutics. “Chief among these milestones was our announcement in September 2020 that the tebipenem HBr ADAPT-PO Phase 3 clinical trial in complicated urinary tract infection (cUTI) and acute pyelonephritis (AP) met its primary endpoint. We look forward to another productive year in 2021, as we advance tebipenem HBr towards an NDA submission in the second half of 2021 and move closer to potentially addressing the unmet needs of the estimated 2.7 million cUTI and AP patients in the United States who may benefit from an oral treatment option that could prevent unnecessary hospitalizations.”

Clinical Highlights and Upcoming Milestones

Tebipenem HBr:

In September 2020, Spero announced positive data from the ADAPT-PO Phase 3 clinical trial demonstrating that oral tebipenem HBr was statistically non-inferior to intravenous ertapenem in the treatment of patients with cUTI and patients with AP with respect to the primary endpoint. The ADAPT-PO clinical trial was the first trial to evaluate an all-oral regimen of tebipenem HBr head-to-head versus an all intravenous (IV) regimen of ertapenem for the treatment of adults with cUTI and AP. The top-line data as well as additional analyses from the trial were subsequently presented at IDWeek in October 2020.

In January 2021, Spero announced that the U.S. Patent and Trademark Office (USPTO) issued U.S. Patent No. 10,889,587, which covers a crystalline formulation of tebipenem HBr. This patent expires in February 2038. Tebipenem HBr has also been granted Qualified Infectious Disease Product (QIDP) and Fast Track designations by the U.S. Food and Drug Administration (FDA) for the treatment of cUTI.

The Phase 1 clinical trials required for a new drug application (NDA) submission to the U.S. Food and Drug Administration (FDA) for tebipenem HBr have also been completed, and Spero remains on track to make an NDA submission to the FDA in the second half of 2021.

SPR720:

In December 2020, Spero initiated a Phase 2a dose-ranging clinical trial of oral SPR720 in patients with nontuberculous mycobacterial pulmonary disease (NTM-PD). The advancement of SPR720 into the Phase 2a clinical trial was based on positive data from a Phase 1 clinical trial that evaluated the safety, tolerability and pharmacokinetics of SPR720, as well as supportive data from a series of non-clinical GLP toxicology and safety pharmacology studies, including investigational new drug application (IND)-enabling 28- and 31-day GLP studies in non-human primates and rats, respectively.

In February 2021, following Spero's notification to the FDA of Spero's decision to pause dosing in its ongoing Phase 2a clinical trial of SPR720 as a precautionary measure related to data from an ongoing toxicology study of SPR720 in adult non-human primates in which mortalities with inconclusive causality to treatment were observed, the FDA issued a verbal notification of a clinical hold on the clinical trial. Subsequently, Spero received a formal clinical hold letter in which the FDA requested additional information from the non-human primate toxicology study, including a study report.

To best facilitate potential adjustments to the Phase 2a SPR720 clinical trial protocol that may be made in the future based on findings from the ongoing toxicology study and FDA feedback, and to avoid incurring costs associated with the clinical trial while it is on hold, Spero has decided to discontinue the Phase 2a clinical trial at this time. Spero continues to work with the FDA to evaluate the non-human primate toxicology study and determine the best development pathway for the SPR720 clinical program.

SPR206:

In January 2020, Spero reported positive Phase 1 clinical trial results for SPR206 in healthy volunteers. Under its agreement with Everest Medicines, Spero received a $2.0 million milestone payment from Everest in the fourth quarter of 2020 for the delivery of the Phase 1 Clinical Study Report. Through its grant from the U.S. Department of Defense awarded in July 2019, and in conjunction with Everest Medicines, Spero continues to expect to initiate a Phase 1 bronchoalveolar lavage (BAL) clinical trial assessing the penetration of SPR206 into the pulmonary compartment in the first half of 2021 and a renal impairment clinical trial of SPR206 in 2021.

Management Highlights

Sath Shukla joined Spero as Chief Financial Officer on January 4, 2021. He brings over 20 years of strategic and financial leadership experience to Spero. Mr. Shukla most recently served as Chief Financial Officer at Ziopharm Oncology, Inc. and previously served as Vice President and Global Head of Corporate Finance for Vertex Pharmaceuticals, Inc.

Tamara Joseph, J.D., L.L.M., joined Spero as Chief Legal Officer on December 2, 2020. She has over 20 years of leadership roles in the biotechnology sector, overseeing legal, public and government affairs, compliance and risk management. Ms. Joseph most recently served as Chief Legal Officer at Millendo Therapeutics, Inc. and previously served as General Counsel at Enzyvant Therapeutics Ltd., InVivo Therapeutics Holdings Corp., Cubist Pharmaceuticals, Inc., Mayne Pharma Ltd., and Transkaryotic Therapies, Inc.

Fourth Quarter and Full Year 2020 Financial Results

Spero reported a net loss for the fourth quarter and year ended December 31, 2020 of $18.6 million and $78.8 million, or $0.68 and $3.52 per common share, respectively. Net loss for the fourth quarter and year ended December 31, 2019 was $25.0 million and $60.9 million, or $1.31 and $3.35 per common share, respectively.

Total revenue for the fourth quarter 2020 of $1.9 million was lower than the $3.6 million for the same period of 2019 and was comprised of reimbursement for its pipeline candidates under collaboration agreements with third parties and grants from various government agencies. Total revenue for the year ended December 31, 2020 was $9.3 million compared to $18.1 million for the year ended December 31, 2019. Total revenue for the fourth quarter and full-year 2020 was lower than the same periods in 2019 due to lower reimbursement under Spero's contract with the Biomedical Advanced Research and Development Authority (BARDA) for qualified tebipenem HBr expenses as well as lower collaboration revenue.

Research and development expenses for the fourth quarter 2020 of $13.2 million were lower than the $25.7 million for the same period of 2019 primarily due to lower expenses for the tebipenem HBr development program following the completion of the ADAPT-PO Phase 3 clinical trial in the third quarter of 2020. Research and development expenses for the year ended December 31, 2020 were $67.0 million compared to $65.8 million for the year ended December 31, 2019, with increased expenses in 2020 compared with 2019 due to greater personnel-related spend to support the pipeline candidates, partially offset by lower spend on the tebipenem HBr and SPR206 programs. Spero expects that its research and development expenses will decrease in 2021 relative to 2020 due to lower direct spend on clinical trial costs following completion of the ADAPT-PO Phase 3 clinical trial.

General and administrative expenses for the fourth quarter 2020 of $7.5 million were higher than the $3.8 million for the same period of 2019, primarily due to increased headcount. General and administrative expenses for the year ended December 31, 2020 were $21.4 million compared to $15.6 million for the year ended December 31, 2019, with the increased expenses in 2020 compared to 2019 primarily due to increased headcount and professional fees to support precommercial activities and growth of the business. Spero expects general and administrative expenses to increase in 2021 relative to 2020 as it builds its commercial capabilities and expands its infrastructure ahead of a potential tebipenem HBr commercial launch in 2022.

As of December 31, 2020, Spero had cash, cash equivalents and marketable securities of $126.9 million. Based on current plans, Spero believes that existing cash, cash equivalents and marketable securities, together with the committed funding from its existing BARDA contract and other non-dilutive funding commitments, will be sufficient to fund its operating expenses and capital expenditure requirements into the second quarter of 2022, including through the submission of the NDA for tebipenem HBr.

Conference Call and Webcast

Spero will host a conference call and webcast today at 4:30 p.m. EST. To access the call, please dial (877) 705-6003 (domestic) or (201) 493-6725 (international) and refer to conference ID 13716494. The conference call will also be webcast live and a link to the webcast can be accessed ***here*** and also 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.

About Spero Therapeutics

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

Spero's lead product candidate, tebipenem HBr (tebipenem pivoxil hydrobromide; formerly SPR994), is being developed as the first oral carbapenem antibiotic for use in complicated urinary tract infections (cUTI) and acute pyelonephritis (AP). In September 2020, Spero announced positive top-line results from its Phase 3 ADAPT-PO clinical trial of tebipenem HBr in cUTI and AP.

Spero is also developing SPR720 as a novel oral therapy product candidate for the treatment of rare, orphan pulmonary disease caused by non-tuberculous mycobacterial (NTM) infections.

Spero also has an IV-administered next generation polymyxin product candidate, SPR206, developed from its potentiator platform, which is being developed to treat MDR Gram-negative infections in the hospital setting.

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

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.

Forward-Looking Statements

This press release may contain forward-looking statements. These statements include, but are not limited to, statements about the initiation, timing and submission to the FDA of a NDA for tebipenem HBr and the potential approval of tebipenem HBr by the FDA; future commercialization, the potential number of patients who could be treated by tebipenem HBr and market demand for tebipenem HBr generally; expected broad access across payer channels for tebipenem HBr; the expected pricing of tebipenem HBr and the anticipated shift from IV to oral administration; the design, initiation, timing, progress and results of Spero's preclinical studies and clinical trials and its research and development programs, including the commencement of Spero's planned Phase 1 bronchoalveolar lavage (BAL) clinical trial assessing the penetration of SPR206 into the pulmonary compartment and its renal impairment study of SPR206; management's assessment of the results of such preclinical studies and clinical trials; the direct and indirect impact of the pandemic caused by an outbreak of a new strain of coronavirus on Spero's business and operations, including manufacturing, research and development costs, clinical trials, regulatory processes and employee expenses; and Spero's cash forecast and anticipated expenses, anticipated payments under Spero's agreement with Everest Medicines, potential payments under Spero's agreement with BARDA, the sufficiency of its cash resources and the availability of additional non-dilutive funding from governmental agencies beyond any initially funded awards. 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 Spero's ability to timely complete related Phase 1 trials for its planned NDA submission for tebipenem HBr, taking into account the possible effects of the COVID-19 pandemic; Spero's need for additional funding; the lengthy, expensive, and uncertain process of clinical drug development; 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 develop and commercialize Spero's product candidates, if approved; the potential impact of the COVID-19 pandemic; Spero's ability to retain key personnel and to manage its growth; whether Spero will satisfy all of the pre-conditions to receipt of the development milestone payment under its agreement with Everest Medicines; whether BARDA elects to exercise its second option under Spero's agreement with BARDA; 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
(Unaudited, Amounts in Thousands, Except Share and Per Share Data)

	Three Months Ended December 31,		Year Ended December 31,	
	2020	2019	2020	2019
Revenues:				
Grant revenue	$ 1,907	$ 2,934	$ 9,072	$ 13,405
Collaboration revenue	—	696	258	$ 4,742
Total revenues	1,907	3,630	9,330	18,147
Operating expenses:				
Research and development	13,205	25,728	67,003	65,775
General and administrative	7,498	3,785	21,440	15,588
Total operating expenses	20,703	29,513	88,443	81,363
Loss from operations	(18,796)	(25,883)	(79,113)	(63,216)
Other income (expense)	211	897	833	2,291
Net loss	$ (18,585)	$ (24,986)	$ (78,280)	$ (60,925)
Deemed dividend	$ —	$ —	$ (549)	$ —
Net loss attributable to common shareholders of Spero Therapeutics, Inc.	$ (18,585)	$ (24,986)	$ (78,829)	$ (60,925)
Net loss per share attributable to common shareholders per share, basic and diluted	$ (0.68)	$ (1.31)	$ (3.52)	$ (3.35)
Weighted average shares outstanding, basic and diluted:	27,369,943	19,052,827	22,386,122	18,160,525

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

	December 31, 2020	December 31, 2019
Cash, cash equivalents and marketable securities	$ 126,906	$ 82,045
Other assets	26,545	24,058
Total assets	**$ 153,451**	**$ 106,103**
Total liabilities	21,411	31,529
Total stockholder's equity	132,040	74,574
Total liabilities and stockholders' equity	**$ 153,451**	**$ 106,103**