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): November 5, 2020

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 November 5, 2020, Spero Therapeutics, Inc. (the "Company") issued a press release announcing its results for the quarter ended September 30, 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.

Exhibit 99.1	Press Release, dated November 5, 2020
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: November 5, 2020

By: /s/ Stephen DiPalma
Stephen DiPalma
Interim Chief Financial Officer and Treasurer

Exhibit 99.1

Spero Therapeutics Announces Third Quarter 2020 Operating Results and Provides Business Update

Achieved key clinical milestones with positive ADAPT-PO Phase 3 data and SPR720 IND acceptance

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

CAMBRIDGE, Mass., November 5, 2020 — 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 third quarter ended September 30, 2020 and provided a business update.

"We made significant clinical progress in the third quarter with the announcement that the ADAPT-PO Phase 3 trial met its primary endpoint," said Ankit Mahadevia, M.D., Chief Executive Officer of Spero Therapeutics. "The ADAPT-PO trial was a rigorous test for tebipenem HBr, having been the first trial ever to test an all oral regimen against an all IV regimen for the treatment of complicated urinary tract infection (cUTI) and acute pyelonephritis (AP). We are excited by the positive results seen in the ADAPT-PO trial, which were presented at IDWeek 2020. These results highlight the potential benefit oral tebipenem HBr could offer to patients with cUTI and AP, who are in need of a new treatment option that may allow them to avoid unnecessary hospitalizations."

Clinical Highlights and Upcoming Milestones

COVID-19 Update:

Spero is committed to advancing its clinical programs while protecting the safety and well-being of patients, physicians and their staff. Spero is monitoring the impact of the COVID-19 pandemic on it business and clinical programs. Spero does not foresee material impacts of the COVID-19 pandemic on its clinical plans at this time and is maintaining its current milestone guidance for its pipeline products.

Tebipenem HBr:

Spero's lead product candidate, tebipenem HBr, has the potential to be the first oral carbapenem antibiotic, if approved, to treat cUTI, including AP. In September 2020, Spero announced positive data from the ADAPT-PO Phase 3 trial evaluating 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, including AP. The ADAPT-PO trial achieved its primary objective, 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 of overall response at the test-of-cure (TOC) visit in the microbiological-intent-to-treat (micro-ITT) population. Overall response (combined clinical cure plus microbiological eradication) rates at TOC were 58.8% for oral tebipenem versus 61.6% for IV ertapenem (treatment difference, -3.3%; 95% confidence interval [CI]: -9.7, 3.2; -12.5% NI margin).

Data presented at IDWeek 2020 expanded on the topline data, and demonstrated that both the clinical cure and microbiological eradication rates were comparable between treatment groups at the end of treatment (EOT), TOC and at the late follow-up (LFU) visits. Specifically, clinical cure rates, which are the key determinant in routine clinical management of cUTI/AP patients, were >93% in both treatment groups at TOC. The high clinical cure rates at TOC were sustained through LFU (88.6% and 90% for tebipenem HBr and ertapenem, respectively), demonstrating a durable clinical response in patients with cUTI and AP. Favorable microbiological response rates at TOC were likewise comparable between treatment groups and were similarly sustained up to LFU in both treatment groups (57.2% and 58.2% for tebipenem HBr and ertapenem, respectively). There were no statistically significant differences between treatment groups in overall response rates across key subgroups of interest, including those determined by age, baseline diagnosis, and presence of bacteremia at baseline. Per pathogen microbiological response rates were generally balanced across treatment groups for the predominant uropathogens. Comparative safety and tolerability data from 1,372 hospitalized adult patients enrolled in the study were similar between the tebipenem HBr and ertapenem treatment groups. Twenty six percent of subjects in both treatment groups experienced one or more treatment-emergent adverse events. The most commonly reported treatment emergent adverse events in both treatment groups were diarrhea (5.7% and 4.4% for tebipenem HBr and ertapenem, respectively) and headache (3.8% in both treatment groups).

Tebipenem HBr has 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. Spero intends to make an NDA submission to the FDA for tebipenem HBr in the second quarter of 2021.

SPR720:

SPR720 is an orally administered antimicrobial agent being developed by Spero for the treatment of non-tuberculous mycobacterial (NTM) disease, a rare orphan disease, as well as other infections, including *Mycobacterium tuberculosis*. Spero announced positive topline data from its Phase 1 clinical trial of SPR720 in healthy volunteers in December 2019. Both the Phase 1 trial and pharmacokinetic/pharmacodynamic (PK/PD) data recently presented at IDWeek 2020 indicated that predicted therapeutic exposures could be attained with a 500 – 1,000 mg once daily oral dose. Spero received acceptance of its IND application for SPR720 in August 2020 and was awarded Fast Track designation for the treatment of adult patients with NTM pulmonary disease by the FDA in September 2020. Spero expects to initiate patient dosing in its dose-ranging Phase 2a clinical trial of SPR720 by year-end 2020.

Spero's Phase 2a clinical trial will be a multi-center, partially blinded, placebo-controlled proof-of-concept clinical trial of SPR720 that will enroll approximately 90 treatment inexperienced patients with NTM pulmonary disease due to *Mycobacterium avium* complex (MAC). Patients will be randomized to receive either 500 mg or 1,000 mg of oral SPR720, placebo or standard of care consisting of a macrolide and ethambutol, plus the option of adding a rifamycin. The

objectives of the trial are to evaluate plasma pharmacokinetics, safety, tolerability, and microbiological response of SPR720 compared with placebo and standard of care over 28 days of treatment.

SPR206:

SPR206 is an IV-administered product candidate being developed as an innovative option to treat multi-drug resistant (MDR) Gram-negative bacterial infections. In January 2020, Spero reported positive Phase 1 clinical trial results for SPR206 in healthy volunteers. Under its agreement with Everest Medicines, Spero expects to receive a $2.0 million milestone payment 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 to initiate a renal impairment study of SPR206 in 2021.

Third Quarter 2020 Financial Results

Spero reported a net loss for the third quarter ended September 30, 2020 of $18.9 million or $0.86 per common share, compared to a net loss of $17.7 million or $0.95 per common share reported for the same period in 2019.

Total revenue for the third quarter of 2020 was $4.0 million, compared with revenues of $4.6 million in the third quarter of 2019, the decrease due primarily to lower reimbursement in the third quarter of 2020 under Spero's contract with the Biomedical Advanced Research and Development Authority (BARDA) for qualified tebipenem HBr expenses.

Research and development expenses for the third quarter of 2020 were $17.7 million, compared with $18.5 million of research and development expenses for the same period of 2019. This year-over-year decrease was due to lower expenses in the tebipenem HBr program following the completion of significant activities in the ADAPT-PO Phase 3 clinical trial. Spero expects to continue to incur expenses related to tebipenem HBr as it finalizes activities in the Phase 3 clinical trial and advances a potential NDA filing for tebipenem HBr.

General and administrative expenses for the third quarter of 2020 of $5.3 million were higher than the $4.1 million reported in the same period of 2019, primarily due to increased headcount and professional fees to support precommercial activities and growth of the business. Spero continues to expect general and administrative expenses to increase to support tebipenem HBr through potential approval, as well as to support Spero's other product candidates.

As of September 30, 2020, Spero had cash and cash equivalents of $127.2 million, inclusive of $74.7 million in aggregate net proceeds from a follow-on offering that closed on September 15, 2020. Subsequent to September 30, 2020, the company raised an additional $11.2 million in net proceeds through the exercise of the overallotment option by the underwriters in the follow-on offering, bringing the total net proceeds from the follow-on offering to $85.9 million. Spero believes that its existing cash, cash equivalents and marketable securities, together with

committed funding from the BARDA contract and other non-dilutive funding commitments, will be sufficient to fund its operating expenses and capital expenditure requirements into the first quarter of 2022, through the approval process for tebipenem HBr.

Upcoming Investor and Clinical Presentations

- Corporate presentation at the Stifel Virtual Healthcare Conference on November 18, 2020 at 10:00 AM ET
- Corporate presentation at the Evercore ISI HealthCONx Virtual Conference on December 3, 2020 at 8:25 AM ET

Conference Call and Webcast

Spero will host a conference call and webcast today at 4:30 p.m. EDT. To access the call, please dial (800) 239-9838 (domestic) or (323) 794-2551 (international) and refer to conference ID 8427958. 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 advancing SPR720, its novel oral therapy product candidate being developed 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 that is being developed to treat MDR 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 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 2a clinical trial of SPR720 and 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.

Spero Investor and Media Contact:
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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 September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Revenues:				
Grant revenue	$ 3,957	$ 4,471	$ 7,165	$ 10,471
Collaboration revenue	38	172	258	$ 4,046
Total revenues	3,995	4,643	7,423	14,517
Operating expenses:				
Research and development	17,706	18,495	53,798	40,047
General and administrative	5,309	4,133	13,942	11,803
Total operating expenses	23,015	22,628	67,740	51,850
Loss from operations	(19,020)	(17,985)	(60,317)	(37,333)
Other income (expense)	84	268	622	1,394
Net loss	$ (18,936)	$ (17,717)	$ (59,695)	$ (35,939)
Deemed dividend	$ —	$ —	$ (549)	$ —
Net loss attributable to common shareholders of Spero Therapeutics, Inc.	$ (18,936)	$ (17,717)	$ (60,244)	$ (35,939)
Net loss per share attributable to common shareholders per share, basic and diluted	$ (0.86)	$ (0.95)	$ (2.91)	$ (2.01)
Weighted average shares outstanding, basic and diluted:	21,933,922	18,659,079	20,712,720	17,859,829

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

	September 30, 2020	December 31, 2019
Cash, cash equivalents and marketable securities	$ 127,244	$ 82,045
Other assets	29,796	24,058
Total assets	**$ 157,040**	**$ 106,103**
Total liabilities	24,251	31,529
Total stockholder's equity	132,789	74,574
Total liabilities and stockholders' equity	**$ 157,040**	**$ 106,103**