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): January 3, 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 8.01. Other Events.

Spero Therapeutics, Inc. (the "Company") issued the press releases attached hereto as Exhibits 99.1 and 99.2 on January 3, 2022 and January 4, 2022, respectively, and they are filed and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1	Press Release titled "Spero Therapeutics Announces FDA Acceptance and Priority Review of New Drug Application for Tebipenem HBr for the Treatment of Complicated Urinary Tract Infections including Pyelonephritis," dated January 3, 2022.
99.2	Press Release titled "Spero Therapeutics Announces Lifting of FDA Clinical Trial Hold on SPR720," dated January 4, 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: January 4, 2022

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

Exhibit 99.1

Spero Therapeutics Announces FDA Acceptance and Priority Review of New Drug Application for Tebipenem HBr for the Treatment of Complicated Urinary Tract Infections including Pyelonephritis

The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date of June 27, 2022

CAMBRIDGE, Mass., January 3, 2022 — Spero Therapeutics, Inc. (Nasdaq: SPRO), today announced that the U.S. Food and Drug Administration (FDA) has granted Priority Review designation and confirmed the acceptance for substantive review of the New Drug Application (NDA) seeking approval for tebipenem HBr oral tablets for treatment in adult patients with complicated urinary tract infections (cUTI), including acute pyelonephritis, caused by susceptible microorganisms. Tebipenem HBr has been granted Qualified Infectious Disease Product (QIDP), Fast Track, and Priority Review designations for these cUTI indications. The Agency is planning to hold an Advisory Committee meeting to discuss this application and has also set a Prescription Drug User Fee Act (PDUFA) target action date of June 27, 2022.

“The FDA acceptance of this NDA is a major step forward in our mission to provide patients the first and only oral carbapenem antibiotic to treat cUTI. If approved, tebipenem HBr may provide patients an oral treatment option, allowing them to potentially either recover at home from their infections or leave the hospital sooner,” said Ankit Mahadevia, M.D., Chief Executive Officer of Spero. “This is an important accomplishment and an exciting moment for all of us at Spero, as we execute our plan on becoming a commercial organization. We are committed to working closely with the FDA throughout the NDA review process and look forward to tebipenem HBr’s anticipated launch in the second half of 2022.”

The NDA submission includes previously communicated positive data from the Phase 3 ADAPT-PO trial. These data showed that ADAPT-PO met its primary endpoint by demonstrating that oral tebipenem HBr was statistically non-inferior to intravenous (IV) ertapenem in the treatment of patients with cUTI and patients with acute pyelonephritis (AP).

David Melnick, M.D., Chief Medical Officer of Spero, added, “ADAPT-PO was rigorously designed both to support this NDA and to provide physicians with the confidence needed to prescribe oral tebipenem HBr to appropriate patients in place of IV therapy, if approved. We believe the positive results from the trial have allowed us to accomplish this first goal and indicate that use of tebipenem HBr may ultimately improve patient care and reduce healthcare resource utilization in cUTI.”

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 cUTI, including pyelonephritis. Tebipenem HBr is an investigational drug in the United States and is currently not approved for the treatment of complicated urinary tract infection, including pyelonephritis.

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

Forward Looking Statements

This press release may contain forward-looking statements. These statements include, but are not limited to, statements about the potential approval of tebipenem HBr by the FDA; the timing of launch of tebipenem HBr; the potential number of patients who could be treated by tebipenem HBr and market demand for tebipenem HBr generally; the effectiveness of tebipenem HBr and its potential impact on healthcare resource utilizations; the anticipated shift from IV to oral administration, and the length of time for which Spero's cash resources are expected to be sufficient. 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 any delays in review of the NDA submission by the FDA for any reason or that the PDUFA date for the NDA review may be revised; including the COVID-19 pandemic; the timing and content of advice given and decisions made by regulators, including the FDA; 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'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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Exhibit 99.2

Spero Therapeutics Announces Lifting of FDA Clinical Trial Hold on SPR720

CAMBRIDGE, Mass., January 4, 2022 — Spero Therapeutics, Inc. (Nasdaq: SPRO), today announced that the U.S. Food and Drug Administration (FDA) has lifted the clinical hold on the Phase 2 trial of SPR720, Spero's investigational oral product candidate being developed for nontuberculous mycobacterial (NTM) disease.

"We are very pleased with the FDA's decision and eager to bring SPR720 back into the clinic," said Ankit Mahadevia, M.D., Chief Executive Officer of Spero. "Extensive analyses, together with prior clinical and non-clinical data, support our belief that SPR720 has the potential to offer a new, well-tolerated, oral treatment option for patients suffering from NTM-PD. We would like to thank the FDA for its guidance and look forward to SPR720's continued clinical development."

David Melnick, M.D., Chief Medical Officer of Spero, added, "Current treatments for nontuberculous mycobacteria are often ineffective and involve lengthy and complex combination regimens that include injectable and/or inhalable antibiotics. Through SPR720's clinical development and potential future marketing approval, we aim to provide appropriate NTM-PD patients with a once-daily oral therapy, in conjunction with existing therapeutic regimens. This has the potential to address a pressing unmet need for an indication that represents a global health concern with increasing incidence."

The SPR720 program was placed on a clinical hold by the FDA following a review of data from a non-human primate (NHP) toxicology study in which mortalities with inconclusive causality to treatment were observed. The FDA's decision to lift the hold follows Spero's submission of a comprehensive study report with detailed analyses from the NHP toxicology study. Spero plans on engaging with the FDA in Q1 of 2022 to discuss the re-initiation of the SPR720 Phase 2 trial for NTM-pulmonary disease (NTM-PD) patients, with an expected study start date commencing in the second half of 2022.

About SPR720

SPR720 represents a novel class of antibacterial agents that target enzymes essential for bacterial DNA replication. It is currently under development as an oral therapy for the treatment of non-tuberculous mycobacterial (NTM) disease, a rare orphan disease. Non-tuberculous mycobacteria are ubiquitous environmental pathogens that can cause progressive lung damage and respiratory failure, particularly in patients with compromised immune systems or underlying pulmonary disorders. Although rare, the incidence of pulmonary NTM disease is increasing worldwide. Treatment of pulmonary NTM disease requires prolonged therapy (continuing for approximately 12 to 24 months) with a combination of mostly unapproved drugs and is frequently complicated by tolerability and/or toxicity issues. Additionally, there are currently no oral antibiotics specifically approved for use to treat pulmonary NTM disease. Thus, if approved, SPR720 has the potential to address an important unmet need as the first oral antibiotic approved for the treatment of this debilitating disease.

SPR720 has been granted Qualified Infectious Disease Product (QIDP) designation by the FDA for the treatment of lung infections caused by non-tuberculous mycobacteria and lung infections caused by *Mycobacterium tuberculosis* (Mtb). It has also received an orphan drug designation from the FDA for the treatment of NTM infection. The FDA has also designated the investigation of SPR720 capsules for treatment of adult patients with NTM-PD a Fast Track development program.

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Tebipenem HBr is an investigational drug in the United States and is currently not approved for the treatment of complicated urinary tract infection, including pyelonephritis.

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

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Forward Looking Statements

This press release may contain forward-looking statements. These statements include, but are not limited to, statements about the plans for Spero's ongoing development of SPR720 and the potential therapeutic and other benefits of Spero's product candidates. 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 the COVID-19 pandemic; the timing and content of advice given and decisions made by regulators, including the FDA; 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'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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