# Spero Therapeutics Provides Update on SPR720 Phase 2a Clinical Trial

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CAMBRIDGE, Mass., Feb. 05, 2021 (GLOBE NEWSWIRE) -- 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 that the United States Food and Drug Administration (FDA) informed Spero that a clinical hold has been placed on its Phase 2a clinical trial of SPR720, Spero's investigational oral antimicrobial agent being evaluated in patients with nontuberculous mycobacterial pulmonary disease (NTM-PD).

Spero received verbal notification of the clinical hold for the SPR720 Phase 2a trial but has not yet received written notice from the FDA. The clinical hold follows the notification by Spero to the FDA of its decision to pause dosing in its ongoing Phase 2a clinical trial of SPR720 as a precautionary measure following events in its ongoing animal toxicology study of SPR720. The decision to implement the pause was made based on a recommendation from Spero's Safety Review Board (SRB), following review of data from an ongoing toxicology study of SPR720 in adult non-human primates in which mortalities with inconclusive causality to treatment were observed. The animal study is being conducted to assess the potential toxicity of SPR720 over a 4-month duration. A concurrent 4-month study of SPR720 in rats is proceeding uneventfully. These studies are meant to support longer-term treatment with SPR720 beyond the 28 days currently supported by IND-enabling toxicology studies. Spero is in discussion with FDA to evaluate the findings and determine the further development pathway for the SPR720 clinical program. No serious adverse events have been observed in any human study participants.

"At Spero, patient safety is of primary importance and we are committed to working with FDA to evaluate findings from our ongoing primate toxicology study in an effort to determine whether these findings are drug-related and what impact, if any, the study may have on the further evaluation of SPR720 in the Phase 2a clinical trial," said Ankit Mahadevia, MD. "Prior, extensive clinical and non-clinical evaluation of SPR720 supports our belief that SPR720, if approved, has the potential to offer a new safe and well-tolerated treatment option for patients suffering from NTM-PD."

Spero initiated the Phase 2a clinical trial (SPR720-201) in December 2020. The trial is designed as a multi-center, partially-blinded, placebo-controlled, proof-of-concept clinical trial of SPR720 with target enrollment of approximately 90 treatment-inexperienced study participants with NTM-PD due to *Mycobacterium avium* complex (MAC). Patients enrolled in the trial are randomized to receive either 500 mg or 1,000 mg of oral SPR720 once daily, placebo, or standard-of-care (SOC), consisting of a macrolide and ethambutol, plus the option of adding a rifamycin.

The safety, tolerability and PK of orally administered SPR720 was previously evaluated in a Phase 1 clinical trial (SPR720-101) that was completed in December 2019, with clinical data presented at Infectious Disease Society of America (IDSA) IDWeek™ 2020 Conference in October 2020. In the Phase 1 clinical trial, SPR720 was given to study participants as single oral doses ranging from 100 mg to 2,000 mg and as repeat total daily doses ranging from 500 mg to 1,500 mg for up to 7 to 14 days. Across seven SAD and five MAD cohorts, a total of 96 healthy volunteers (including a cohort of healthy elderly (age ≥ 65 years) volunteers) were randomized to receive SPR720 or placebo. Data indicated that SPR720 was generally well-tolerated at doses up to 1,000 mg daily over the maximum studied duration of 14 days. There were no serious adverse events reported in the Phase 1 clinical trial and all participants completed the trial.

SPR720 has also been assessed in a series of completed non-clinical GLP toxicology and safety pharmacology studies, including IND-enabling 28- and 31-day GLP studies in non-human primates and rats, respectively. There were no remarkable findings observed in these completed studies and the results supported the advancement of SPR720 into the now complete Phase 1 trial and the current Phase 2a clinical trial that is being conducted under the in-effect IND pursuant to institutional review board oversight.

**About SPR720**

SPR720 represents a novel class of antibacterial agents that target enzymes essential for bacterial DNA replication. SPR720 was acquired from Vertex and is currently under development by Spero as an oral therapy for the treatment of non-tuberculous mycobacterial (NTM) disease, a rare orphan disease. NTM 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.

Spero believes that its intellectual property portfolio for SPR720 will provide protection globally, including in the United States and Europe, through 2033. 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) and orphan drug designation from the FDA for the treatment of nontuberculous mycobacterial (NTM) infection. The investigation of SPR720 capsule for treatment of adult patients with NTM-PD has also been designated as a Fast Track development program by the FDA.

**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, the potential approval of tebipenem HBr by the FDA and commercialization of tebipenem HBr, 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 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, complete studies and clinical trials for and commercialize Spero's product candidates, if approved; the outcome of discussions with the FDA regarding the Phase 2a clinical trial of SPR720 and Spero's ability to proceed with such trial; the potential impact of the COVID-19 pandemic; Spero's ability to retain key personnel and to manage its growth; Spero's ability to maintain and enforce its intellectual property; 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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