Spero Therapeutics Announces First Patient Dosed with SPR720 in Phase 2a Clinical Trial in Patients with Nontuberculous Mycobacterial Pulmonary Disease

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CAMBRIDGE, Mass., Dec. 10, 2020 (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 (MDR) bacterial infections, today announced that it has initiated dosing in patients with nontuberculous mycobacterial pulmonary disease (NTM-PD) in its dose-ranging Phase 2a clinical trial of SPR720, Spero's oral antimicrobial agent in development for the treatment of NTM-PD.

"The initiation of this trial is a significant milestone for the program, and we look forward to the trial producing important data that will further inform our development pathway for SPR720 in NTM-PD," said Ankit Mahadevia, M.D., Chief Executive Officer of Spero Therapeutics. "The lack of approved, oral options for the treatment of NTM-PD presents a significant unmet need for patients and we believe SPR720 has the potential to offer a new treatment option."

The Phase 2a clinical trial is a multi-center, partially blinded, placebo-controlled proof-of-concept clinical trial of SPR720 that will enroll approximately 90 treatment-inexperienced patients with NTM-PD due to *Mycobacterium avium* complex (MAC). Patients will be 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 objectives of the trial are to evaluate the plasma pharmacokinetics, safety, tolerability, and microbiological response of SPR720 compared with placebo and SOC over 28 days of treatment, with the inclusion of the SOC arm to assess and ensure assay sensitivity for the trial design.

"A significant unmet medical need exists for safe and effective treatments for patients with NTM pulmonary disease. We have very few antibiotics to combat these highly drug resistant organisms, and we essentially lack any approved therapies for first-line therapy against pulmonary NTM," said Dr. Kevin Winthrop, the trial's Principal Investigator and Professor of Infectious Disease and Public Health at Oregon Health and Science University. "Oral SPR720 shows potential to benefit patients with NTM pulmonary disease and we are excited to have initiated this novel Phase 2a trial to assess SPR720 in patients with early onset pulmonary disease."

The Phase 2a clinical trial is supported by data from its first-in-human Phase 1 clinical trial of SPR720 in healthy volunteers and pharmacokinetic/pharmacodynamic (PK/PD) data that was presented at Infectious Disease Society of America (IDSA) IDWeek 2020. That data suggested that predicted therapeutic exposures could be attained with a 500 – 1,000 mg once daily oral dose. Spero expects to report top-line data from the Phase 2a clinical trial in the first half of 2022.

About SPR720

SPR720 represents a novel class of antibacterial agents that target enzymes essential for bacterial DNA replication. SPR720 was acquired from Vertex Pharmaceuticals and is currently under development by Spero as an oral therapy for the treatment of nontuberculous mycobacterial (NTM) pulmonary disease, a rare chronic 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 NTM pulmonary disease is increasing worldwide. Treatment of NTM pulmonary disease requires prolonged therapy (continuing for approximately 12 to 24 months) with a combination of drugs approved for other infections and is frequently complicated by tolerability and/or toxicity issues. There are currently no oral antibiotics specifically approved for use to treat NTM pulmonary disease. Thus, if successfully developed, SPR720 has the potential to address an important unmet need as the first oral antibiotic approved for the treatment of this debilitating disease. Under Spero's collaboration with the Bill and Melinda Gates Medical Research Institute, SPR720 will also be developed for the treatment of *Mycobacterium tuberculosis* (Mtb) infections in select economically disadvantaged countries. Tuberculosis is a priority pathogen as defined by the World Health Organization with it being one of the top ten causes of death worldwide, and a situation where resistance is increasing, and current treatment approaches are not optimal.

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 orphan drug designation by the U.S. Food and Drug Administration (FDA) for the treatment of nontuberculous mycobacterial (NTM) infection. It has also 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), which offers an additional five-year extension of Hatch-Waxman Act exclusivity. The FDA accepted Spero's investigational new drug application (IND) for SPR720 in August 2020 and SPR720 was awarded Fast Track designation for the treatment of adult patients with NTM pulmonary disease by the FDA in September 2020.

SPR720 Research Support
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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 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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