Spero Therapeutics Announces SPR720 Phase 2a Interim Results and Provides a Business Update

Phase 2a proof-of-concept study of SPR720 for the treatment of Nontuberculous Mycobacterial Pulmonary Disease (NTM-PD) did not meet its primary endpoint, based on planned interim analysis of 16 patients

Phase 3 PIVOT-PO trial of tebipenem HBr remains on track for enrollment completion in 2H 2025

Cash runway extended into mid-2026 following a reduction in workforce and restructuring of operations; Unaudited Q3 2024 ending cash balance of $76.3M

CAMBRIDGE, Mass., Oct. 29, 2024 (GLOBE NEWSWIRE) -- Spero Therapeutics, Inc. (Nasdaq: SPRO), a multi-asset clinical-stage biopharmaceutical company, focused on identifying and developing novel treatments for rare diseases and multi-drug resistant (MDR) bacterial infections, today announced that a planned interim analysis of the Phase 2a proof-of-concept study of SPR720 for the treatment of NTM-PD demonstrated that the program did not meet its primary endpoint. While the data showed antimicrobial activity associated with SPR720, the interim analysis did not show sufficient separation from placebo and highlighted potential dose limiting safety issues in subjects dosed at 1,000 mg orally once daily, including three cases of reversible grade 3 hepatotoxicity. In evaluating the totality of both the efficacy and safety data, the Company has elected to suspend its current development program for SPR720 and will evaluate other potential paths forward as the remaining data are collected and analyzed.

As a result of the suspension of the current SPR720 development program, Spero will undergo a restructuring and reduction in force of approximately 39%, which will extend cash runway and support operations into mid-2026, to further support the development of tebipenem HBr, SPR206, and potential strategic activities.

"Spero launched its proof-of-concept clinical study for SPR720 as a monotherapy to evaluate its potential efficacy and safety in treating NTM-PD. While a planned interim analysis provided evidence of antimicrobial activity, the trial unfortunately did not meet the primary endpoint," said Sath Shukla, Spero's President and Chief Executive Officer. "We are therefore suspending development of the SPR720 program and making adjustments to our organization accordingly. I want to offer my sincere thanks to all our Spero SPR720 colleagues, along with our investigators and patients, for their dedication in seeking new treatment options for this devastating disease. We remain committed to bringing forward new treatment options for patients in need, as we continue to advance our tebipenem HBr and SPR206 programs."

Restructuring to Prioritize Programs and Capital Allocation

Spero closed the third quarter ended September 30, 2024, with an unaudited cash estimate of $76.3 million. Following the reduction in force and restructuring, Spero estimates that its existing cash and cash equivalents, together with earned and non-contingent development milestone payments from GSK, as well as other non-dilutive funding commitments, will be sufficient to fund its operating expenses and capital expenditures into mid-2026. During this period, the Company remains focused on advancing tebipenem HBr in the ongoing global PIVOT-PO Phase 3 clinical trial and preparing for a Phase 2 clinical trial for SPR206 contingent on continued non-dilutive funding.

SPR720

SPR720 is an oral, chemically stable phosphate ester prodrug that is converted rapidly in vivo to SPR719, the active moiety. SPR719 targets the ATPase site of DNA gyrase B in mycobacteria, a mechanism that is distinct from that of other antibiotics in use for Non Tuberculous Mycobacterial-Pulmonary Disease (NTM-PD).

Recent updates:

- Phase 2a trial - enrollment concluded in July 2024, with 25 non-refractory patients enrolled in the proof-of-concept trial evaluating SPR720 in NTM-PD. A planned interim analysis based on 16 patients indicated the trial did not meet its primary endpoint of differentiation from placebo in the rate of change in $\log_{10}$ colony forming units per milliliter (CFU/mL). In addition, analysis of the full 25 patient safety data highlighted potential dose limiting safety issues in patients dosed at 1,000mg orally once daily, including three cases of reversible grade 3 hepatotoxicity. The Company plans to complete data analysis of all enrolled patients (n=25) and determine the next steps for the SPR720 program over the next several months. For more information on the trial, see ClinicalTrials.gov identifier NCT05496374.

Tebipenem HBr

Tebipenem HBr is an investigational oral carbapenem antibiotic being developed for the treatment of cUTI including acute pyelonephritis (AP) to help patients avoid hospitalizations or reduce duration of in-patient therapy. Spero granted GSK an exclusive license to commercialize tebipenem HBr in all territories, except certain Asian territories. Spero received $66 million upfront from GSK when the license agreement was signed in 2022, $30 million when the Company reached the Special Protocol Assessment milestone in Q3 2023, and was entitled to receive $95 million in development milestones upon enrollment of the first patient in the PIVOT-PO Phase 3 trial, $47.5 million of which have been received thus far. Spero is further eligible to receive up to $400 million in development, sales, and commercial milestones payments, as well as low single-digit to low double-digit tiered royalties on net product sales.

- Enrollment on track in PIVOT-PO, the global Phase 3 clinical trial of tebipenem HBr in patients with cUTI. This randomized, double-blinded trial compares oral tebipenem HBr with intravenous imipenem cilastatin, in hospitalized adult patients with cUTI/AP. The primary endpoint is overall response (a combination of clinical cure and favorable microbiological response) at the Test-of-Cure (TOC) visit. Target enrollment for the trial is approximately 2,648 patients, with enrollment completion expected in the second half of 2025. For more information on PIVOT-PO, refer to ClinicalTrials.gov ID NCT06059846.

SPR206

SPR206 is an investigational, intravenously administered next-generation polymyxin that has shown antibiotic activity against MDR Gram-negative pathogens, including carbapenem-resistant *Enterobacterales*, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in preclinical studies.

- The U.S. Food and Drug Administration (FDA) cleared the Company's IND for a Phase 2 trial in participants with hospital-acquired or ventilator-associated bacterial pneumonia (HABP/VABP). The Company maintains its guidance to initiate the trial, contingent on availability of non-dilutive funding.

About Spero Therapeutics

Spero Therapeutics, headquartered in Cambridge, Massachusetts, is a multi-asset clinical-stage biopharmaceutical company focused on identifying and developing novel treatments for rare diseases and MDR bacterial infections with high unmet need. For more information, visit www.sperotherapeutics.com

Forward Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, the timing, progress and results of the Company's preclinical studies, clinical trials and research and development programs; management's assessment of the results of such preclinical studies and clinical trials; and the expected cost-savings from the Company's reduction in workforce and restructuring of its operations, the Company's anticipated expenses and its anticipated cash runway . In some cases, forward-looking statements may be identified by terms such as "may," "will," "should," "expect," "plan," "aim," "anticipate," "could," "intent," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue," the negative of these terms or other similar expressions. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of important risks, uncertainties and

other factors that may cause actual results to differ materially from those indicated by such forward looking statements, including whether tebipenem HBr, SPR720 and SPR206 will advance through the clinical trial process on a timely basis, or at all, taking into account the effects of possible regulatory delays, slower than anticipated patient enrollment, manufacturing challenges, clinical trial design and clinical outcomes; whether the results of such trials will warrant submission for approval from the FDA or equivalent foreign regulatory agencies; whether the FDA will ultimately approve tebipenem HBr and, if so, the timing of any such approval; whether the FDA will require any additional clinical data or place labeling restrictions on the use of tebipenem HBr that would delay approval and/or reduce the commercial prospects of tebipenem HBr; whether a successful commercial launch can be achieved and market acceptance of tebipenem HBr can be established; 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; Spero's need for additional funding; the ability to commercialize Spero's product candidates, if approved; Spero's ability to retain key personnel; Spero's leadership transitions; 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 SEC. The forward-looking statements included in this press release represent Spero's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Spero explicitly disclaims any obligation to update any forward-looking statements.

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