



Spero Therapeutics Announces First Patient, First Visit for Phase 3 PIVOT-PO Trial Evaluating Tebipenem HBr in Complicated Urinary Tract Infections

\$95 million in development milestones payable over two years, as part of GSK license agreement

CAMBRIDGE, Mass., Jan. 02, 2024 (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 rare diseases and multi-drug resistant (MDR) bacterial infections, announced today the first patient, first visit for PIVOT-PO, a global pivotal Phase 3 clinical trial of tebipenem HBr in patients with complicated urinary tract infections (cUTI), including acute pyelonephritis (AP). Spero is entitled to receive \$95 million in development milestone payments from GSK, which is payable in four equal installments over two years.

"First patient visit, in the PIVOT-PO Phase 3 clinical trial, is an important milestone in our tebipenem HBr program," said Sath Shukla, President and CEO of Spero Therapeutics. "We are developing Tebipenem HBr to potentially be the first oral broad-spectrum carbapenem in the U.S. for use in patients with cUTI. Oral administration may provide physicians with an alternative to hospital-based IV therapy, for appropriate patients, with potential value to the broader healthcare system."

PIVOT-PO is a global, randomized, double-blind, pivotal Phase 3 clinical trial of oral tebipenem HBr vs. IV imipenem cilastatin, in hospitalized adult patients with cUTI/AP. Patients are being randomized 1:1 to receive tebipenem HBr (600 mg) orally every six hours, or imipenem cilastatin (500 mg) IV every six hours, for a total of seven to ten days. The primary efficacy endpoint will be overall response (composite of clinical cure plus microbiological eradication) at the test-of-cure visit. The primary analysis for the trial will be an assessment of non-inferiority (NI) in the microbiological intention-to-treat population, based on a 10% NI margin. The trial is designed to enroll approximately 2,648 patients, with randomization stratified by age, baseline diagnosis (cUTI or AP), and the presence or absence of urinary tract instrumentation. For further details on the trial, refer to [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT06059846) identifier [NCT06059846](https://clinicaltrials.gov/ct2/show/study/NCT06059846).

The FDA has indicated that positive and persuasive results from PIVOT-PO, supported with confirmatory evidence of efficacy, could be sufficient to support approval of tebipenem HBr as a treatment for cUTI, including pyelonephritis, for a limited use indication.

Under the terms of its license agreement with GSK, Spero is also eligible to receive the following milestone/royalty payments: (1) an additional \$25 million in development milestones; (2) up to \$150 million in potential commercial milestones based on first commercial sale; (3) up to \$225 million in potential sales-based milestones; and (4) low-single digit to low-double digit tiered royalties on net product sales of tebipenem HBr in all territories, except Japan and certain other Asian countries. Additional information on the license agreement is available [here](#).

About Tebipenem HBr

Tebipenem HBr (tebipenem pivoxil hydrobromide; formerly SPR994) is Spero's novel late-stage development asset, an oral formulation of tebipenem pivoxil, a carbapenem antibiotic of the β -lactam class marketed by Meiji Seika Pharma Co. Ltd. (Meiji) in Japan as Orapenem[®] since 2009 for pediatric infections limited to pneumonia, otitis media and sinusitis. Carbapenems are an important subclass of antibiotics because they have been observed to be safe and effective in the treatment of drug-resistant Gram-negative bacterial infections. Tebipenem HBr is being developed for the treatment of complicated urinary tract infections, including AP, caused by certain microorganisms. If approved, tebipenem HBr may be the first oral carbapenem antimicrobial to receive marketing approval in the United States. Tebipenem HBr has been granted Qualified Infectious Disease Product (QIDP) and Fast Track designations by the US

Food and Drug Administration (FDA) for the treatment of cUTI and AP.

Tebipenem HBr Research Support

Select tebipenem HBr studies have been funded in part with federal funds from the U.S. Department of Health and Human Services; Administration for Strategic Preparedness and Response; Biomedical Advanced Research and Development Authority, under contract number HHSO100201800015C.

About Spero Therapeutics

Spero Therapeutics, headquartered in Cambridge, Massachusetts, is a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing, and commercializing novel treatments for bacterial infections, including multi-drug resistant bacterial infections and rare diseases.

- Spero Therapeutics is developing SPR720 as a novel oral therapy candidate for the treatment of a rare, orphan pulmonary disease caused by non-tuberculous mycobacterial infections.
- Tebipenem HBr is an investigational drug in the United States being developed for the treatment of cUTI, including pyelonephritis, caused by certain bacteria, in adult patients who have limited treatment options; tebipenem HBr is not FDA-approved.
- Spero Therapeutics also has an IV-administered next generation polymyxin product candidate, SPR206, developed from its potentiator platform, which is in development 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 design, initiation, timing, progress and results of Spero's preclinical studies and clinical trials and its research and development programs, as well as the regulatory path forward for tebipenem HBr and potential FDA approval, the potential commercialization of tebipenem HBr and its future value, and the potential receipt under the GSK license agreement of milestone payments and royalties on future sales of tebipenem HBr. 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 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 ongoing 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 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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