PIVOT-PO Phase 3 Data Show Tebipenem HBr's Potential as the First Oral Carbapenem Antibiotic for Patients with Complicated Urinary Tract Infections (cUTIs)

- *Data presented at IDWeek 2025 after study stopped early for efficacy*
- *Primary endpoint met, demonstrating non-inferiority of oral tebipenem HBr compared to intravenous treatment*[1]
- *Data will be shared with regulatory authorities to support regulatory filings*

CAMBRIDGE, Mass., Oct. 21, 2025 (GLOBE NEWSWIRE) -- Spero Therapeutics, Inc. (Nasdaq: SPRO) and GSK plc (LSE/NYSE: GSK) today announced efficacy and safety results of the positive pivotal phase 3 PIVOT-PO trial evaluating tebipenem HBr, an investigational oral treatment for complicated urinary tract infections (cUTIs), including pyelonephritis (NCT06059846). These results were presented on October 20, 2025, in a late-breaking oral abstract session at IDWeek 2025 in Atlanta, Georgia.

Complicated UTIs represent an important health issue, with an estimated 2.9 million cases of cUTIs treated annually in the U.S. alone.[2] These infections are often caused by multidrug-resistant pathogens[3] and carry serious risks including organ failure, sepsis, and even death.[3-5] They also result in significant emergency department visits and hospitalizations, contributing to over $6 billion per year in healthcare costs.[6] Current standard of care includes carbapenem antibiotics in cases of sepsis or resistance to other antibiotics, but they are only available for intravenous administration.[7, 8]

The trial, which was stopped early for efficacy in May this year, demonstrated non-inferiority of tebipenem HBr compared to intravenous imipenem-cilastatin in hospitalized patients with cUTI, including pyelonephritis, based on the overall response (composite of clinical cure plus microbiological eradication of the bacteria causing the infection) at the test of cure visit. Tebipenem HBr (oral, 600 mg) achieved a 58.5% overall success rate (261/446 participants) compared to 60.2% overall success rate (291/483 participants) for imipenem-cilastatin (intravenous, 500 mg) (adjusted treatment difference: 1.3%; 95% CI: 7.5%, 4.8%). The safety profile of tebipenem HBr was generally similar to that of other carbapenem antibiotics. The most frequently reported adverse events (in 3% of patients who received tebipenem HBr) were diarrhea and headache; these events were all mild or moderate and non-serious.

Tony Wood, Chief Scientific Officer, GSK, said**:** "Complicated UTIs can have serious consequences for patients, including organ failure and sepsis, and oral options for drug-resistant infections are limited. These ground-breaking data show for the first time that cUTIs, including pyelonephritis, can be treated with an oral carbapenem antibiotic as effectively as with an intravenous one. We have a long-standing commitment to delivering novel anti-infectives and are delighted to offer the potential of tebipenem HBr as an effective oral alternative that could be taken at home."

Esther Rajavelu, Chief Executive Officer, Spero Therapeutics, said: "These data presented at IDWeek represent the culmination of years of dedicated work by our team in close collaboration with GSK. We are deeply grateful to the physicians, researchers, support staff, and, most importantly, to the patients who made this study, and the ones before it, possible. Along with GSK, we are now focused on advancing tebipenem HBr toward FDA submission and bringing this important therapy to patients in need."

Dr George Sakoulas, Infectious Disease specialist, Sharp Memorial Hospital in San Diego, commented: "Increasing antibiotic resistance among community-acquired bacteria that cause complicated urinary tract infections is greatly amplifying the burden of treatment for patients, clinicians, and payers. The therapeutic flexibility of a new oral antibiotic may reduce the need for intravenous antibiotics to treat cUTI, providing benefit to patients and improving

treatment options."

Secondary endpoints also show:

- Clinical cure (i.e. absence of symptoms) rates at test of cure visit were 93.5% in the tebipenem HBr group (417/446) compared to 95.2% in the imipenem-cilastatin group (460/483) with adjusted treatment difference: 1.6% (95% CI: 4.7%, 1.4%)
- Microbiological response rates at test of cure visit were 60.3% in the tebipenem HBr group (269/446) compared to 61.3% in the imipenem-cilastatin group (296/483) with adjusted treatment difference: 0.8% (95% CI: 6.9%, 5.3%)
- Overall, clinical and microbiological response rates at test of cure in participants with infections caused by antimicrobial-resistant Enterobacterales were consistent with the respective response rates in the primary analysis population.

Spero has licensed tebipenem HBr to GSK for development and commercialization in all markets except certain Asian territories. GSK plans to work with US regulatory authorities to include the data as part of a filing in Q4 2025. If approved, tebipenem HBr would be the first oral carbapenem antibiotic in the US for patients who suffer from cUTIs, adding to GSK's growing anti-infectives portfolio and helping address the challenges of antimicrobial resistance (AMR).

The development of tebipenem HBr is supported 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 (BARDA), under contract number HHSO100201800015C.

About tebipenem HBr

Tebipenem pivoxil as hydrobromide salt (Tebipenem HBr) is a late-stage development asset developed in collaboration with Spero Therapeutics. Tebipenem HBr is being developed to treat cUTIs, including pyelonephritis. In September 2022, GSK entered into an exclusive license agreement with Spero Therapeutics for the development and commercialization of tebipenem HBr in all markets, except certain Asian territories. Under this agreement GSK has sub-licensed back to Spero Therapeutics the rights and responsibility to conduct certain development work including the PIVOT-PO Phase 3 study, after which sponsorship of the new drug application (NDA) will be transferred to GSK from Spero Therapeutics. Tebipenem HBr has received Qualified Infectious Disease Product (QIDP) and Fast Track designations from the U.S. Food and Drug Administration (FDA).

About the PIVOT-PO trial

PIVOT-PO was a global, randomized, double-blind, pivotal, non-inferiority (NI margin: -10%) Phase 3 clinical trial of oral tebipenem HBr compared to IV imipenem-cilastatin, in hospitalized adult patients with cUTI including pyelonephritis. Patients were randomized 1:1 to receive tebipenem pivoxil (600 mg) orally every six hours, or imipenem-cilastatin (500 mg) IV every six hours, for a total of seven to ten days. Matching placebos were used to maintain blinding. The primary efficacy endpoint was overall response (composite of clinical cure plus microbiological eradication) at the test-of-cure visit (about 17 days from first dose administration of study drug) in patients with qualifying pathogens susceptible to imipenem. The trial enrolled a total of 1,690 patients, with randomization stratified by age, baseline diagnosis (cUTI or pyelonephritis), and the presence or absence of urinary tract instrumentation. For further details on the trial, refer to clinicaltrials.gov identifier NCT06059846.

About complicated urinary tract infections (cUTIs)

cUTIs are broadly described as any UTI that carries an increased risk of morbidity and mortality.[3] Definitions of cUTIs are not currently uniform among international societies and regulatory agencies.[5, 9] cUTIs encompass a heterogeneous patient population due to the wide range of host factors, comorbidities and urological abnormalities associated with cUTIs.[5, 9] Risk factors for cUTI include indwelling catheters, ureteric stents, neurogenic bladder, obstructive uropathy, urinary retention, urinary diversion, kidney stones, diabetes mellitus, immune deficiency, urinary tract modification, and UTIs in renal transplant patients.[3, 10-13]

About GSK

GSK is a global biopharma company with a purpose to unite science, technology, and talent to get ahead of disease together. Find out more at gsk.com.

About Spero Therapeutics

Spero Therapeutics, headquartered in Cambridge, Massachusetts, is a clinical-stage biopharmaceutical company focused on identifying and developing novel treatments for rare diseases and multi-drug resistant (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, statements regarding the progress and results of Spero's Phase 3 PIVOT-PO trial; the timing of a planned FDA filing in 2H 2025 for tebipenem HBr; the potential of tebipenem HBr to be the first oral carbapenem antibiotic for U.S. patients with cUTI, including pyelonephritis; the potential receipt of milestone payments under Spero's license and collaboration agreements; and the potential benefits of any of Spero's current or future product candidates in treating patients. 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 will advance through the clinical development process, 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, including, in the case of tebipenem HBr, Spero's reliance on GSK pursuant to the exclusive GSK License Agreement to develop tebipenem HBr and GSK's right thereunder to determine whether to further develop tebipenem HBr; 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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