RNS Number : 3973K
GSK PLC
28 May 2025

Issued: 28 May 2025, London UK

PIVOT-PO phase III study for tebipenem HBr stopped early for efficacy following review by Independent Data Monitoring Committee

- If approved, tebipenem HBr could be the first oral carbapenem antibiotic for US patients with complicated urinary tract infections (cUTIs)
- Data to be part of a planned US FDA filing in H2 2025
- An estimated 2.9 million cases of cUTIs are treated annually in the US[1] with many cases requiring hospitalisation, contributing to over 6 billion per year in healthcare costs[2]
- GSK's second anti-infective programme stopped early for efficacy in Phase III after EAGLE 2 and 3 for gepotidacin[3]

GSK plc (LSE/NYSE: GSK) and Spero Therapeutics today announced that the pivotal phase III PIVOT-PO trial evaluating tebipenem HBr, an investigational oral treatment for complicated urinary tract infections (cUTIs), including pyelonephritis, will stop early for efficacy (NCT06059846). The decision follows a recommendation from an Independent Data Monitoring Committee (IDMC), based on a planned interim analysis of data from 1,690 patients enrolled in the study. If approved, tebipenem HBr would be the first oral carbapenem antibiotic for patients in the US who suffer from cUTIs, adding to GSK's innovative anti-infectives portfolio and helping address the challenges of antimicrobial resistance (AMR).

The trial met the primary endpoint of non-inferiority of tebipenem HBr compared to intravenous imipenem-cilastatin in hospitalised adult patients with cUTI, including pyelonephritis, on overall response (composite of clinical cure plus microbiological eradication) at the test-of-cure visit. The IDMC review did not identify any new safety concerns beyond what has been reported in other studies with tebipenem, with diarrhea and headache as the two most reported adverse events. GSK plans to work with US regulatory authorities to include the data as part of a filing in H2 2025. Full results will be submitted for presentation at an upcoming scientific congress and for publication in a peer-reviewed journal.

Tony Wood, Chief Scientific Officer, GSK, said**:** "Complicated UTIs can have a profound impact on patients and carry a high risk of clinical complications, including sepsis and septic shock.[4],[5],[6] Currently many need hospital-based intravenous treatment due to limited oral options for drug-resistant infections, contributing to over 6 billion per year in US healthcare costs[2]. These positive results add to our growing anti-infectives portfolio and reinforce the potential of tebipenem HBr as an effective oral alternative taken at home".

An estimated 2.9 million cases of cUTIs are treated annually in the US alone.[1] These infections are often caused by multidrug-resistant pathogens[1] and carry increased risk of morbidity and mortality.[4,7] Current standard of care includes carbapenem antibiotics, especially in case of sepsis and allergies or resistance to other antibiotics, but they are only available for IV administration. This results in significant emergency department visits and hospitalisations.[6],[7],[8]

Esther Rajavelu, Chief Executive Officer, Spero Therapeutics, said: "We're proud of today's positive result for patients diagnosed with cUTI, including pyelonephritis, where oral treatments are much needed. We look forward to working with GSK on next steps for tebipenem HBr, and would like to thank the patients, investigators, and other clinical staff who have participated in PIVOT-PO trial to reach this advanced stage."

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. It is GSK's second anti-infective programme to be stopped early for efficacy in Phase III, following the EAGLE 2 and EAGLE 3 trials for gepotidacin in 2022.[3]

About tebipenem HBr

Tebipenem pivoxil hydrobromide (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 commercialisation 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 III 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 US FDA.

About the PIVOT-PO trial

PIVOT-PO is a global, randomised, double-blind, pivotal Phase III clinical trial of oral tebipenem pivoxil HBr compared to IV imipenem, in hospitalised adult patients with cUTI including pyelonephritis. Patients were randomised 1:1 to receive tebipenem pivoxil (600 mg) orally every six hours, or imipenem-cilastin (500 mg) IV every six hours, for a total of seven to ten days. Matching placebos are used to maintain blinding. The primary efficacy endpoint is overall response (composite of clinical cure plus microbiological eradication) at the test-of-cure visit. The primary analysis for the trial is an assessment of non-inferiority in the primary analysis population. The trial enrolled a total of 1690 patients, with randomisation 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.[4] Definitions of cUTIs are not currently uniform among international societies and regulatory agencies.[9] cUTIs encompass a heterogeneous patient population due to the wide range of host factors, comorbidities and urological abnormalities associated with cUTIs.[4,9] 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.[10]

GSK in infectious diseases

GSK has pioneered innovation in infectious diseases for over 70 years, and the Company's pipeline of medicines and vaccines is one of the largest and most diverse in the industry, with a goal of developing preventive and therapeutic treatments for multiple disease areas or diseases with high unmet needs globally. Our expertise and capabilities in infectious disease strongly position us to help prevent disease and mitigate the challenge of antimicrobial resistance (AMR).

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

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.

GSK enquiries

Media:	Tim Foley	+44 (0) 20 8047 5502	(London)
	Sarah Clements	+44 (0) 20 8047 5502	(London)
	Kathleen Quinn	+1 202 603 5003	(Washington DC)
	Alison Hunt	+1 540 742 3391	(Washington DC)
Investor Relations:	Constantin Fest	+44 (0) 7831 826525	(London)
	James Dodwell	+44 (0) 20 8047 2406	(London)
	Mick Readey	+44 (0) 7990 339653	(London)
	Steph Mountifield	+44 (0) 7796 707505	(London)
	Jeff McLaughlin	+1 215 751 7002	(Philadelphia)
	Frannie DeFranco	+1 215 751 3126	(Philadelphia)

Registered Office:

79 New Oxford Street

London

WC1A 1DG

References

[1] Carreno JJ, et al. Longitudinal, Nationwide, Cohort Study to Assess Incidence, Outcomes, and Costs Associated With Complicated Urinary Tract Infection. *Open Forum Infect Dis*. 2019;6:ofz446.

[2] Lodise TP, et al. Hospital admission patterns of adult patients with complicated urinary tract infections who present to the hospital by disease acuity and comorbid conditions: How many admissions are potentially avoidable? *Am J Infect Control*. 2021;49(12):1528-1534.

[3] GSK press release, 3 November 2022 - available at: https://www.gsk.com/en-gb/media/press-releases/gsk-announces-phase-iii-trials-for-gepotidacin/

[4] Sabih A, Leslie SW. Complicated urinary tract infections. *StatPearls*. 2023. StatPearls Publishing: Treasure Island, FL, USA.

[5] Zilberberg MD, et al. Descriptive Epidemiology and Outcomes of Hospitalisations With Complicated Urinary Tract Infections in the United States, 2018. *Open Forum Infect Dis*. 2022;9:ofab591.

[6] Li HK, et al. An Unsupported Preference for Intravenous Antibiotics. *PLoS Med*. 2015;12:e1001825.

[7] Vallejo-Torres L, et al. Cost of hospitalised patients due to complicated urinary tract infections: a retrospective observational study in countries with high prevalence of multidrug-resistant Gram-negative bacteria: the COMBACTE-MAGNET, RESCUING study. *BMJ Open*. 2018;8:e020251.

[8] Lodise TP, et al. Retrospective Cohort Study of the 12-Month Epidemiology, Treatment Patterns, Outcomes, and Health Care Costs Among Adult Patients With Complicated Urinary Tract Infections. *Open Forum Infect Dis*. 2022;9:ofac307.

[9] Marantidis J, Sussman RD. Unmet Needs in Complicated Urinary Tract Infections: Challenges, Recommendations, and Emerging Treatment Pathways. *Infect Drug Resist*. 2023:16:1391-1405.

[10] Gomila A, et al. Predictive factors for multidrug-resistant gram-negative bacteria among hospitalised patients with complicated urinary tract infections. *Antimicrob Resist Infect Control*. 2018;7:111.

END

MSCPKFBPOBKKNPB