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Gepotidacin accepted for priority review by US FDA for treatment of uncomplicated urinary tract infections in female adults and adolescents

- Application supported by positive results from pivotal phase III EAGLE-2 and EAGLE-3 trials
- March 26, 2025 assigned as action date for FDA decision
- Gepotidacin could be the first new class of oral antibiotic treatment for uUTIs in over 20 years

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GSK plc (LSE/NYSE: GSK) today announced that the US Food and Drug Administration (FDA) has accepted the New Drug Application (NDA) for gepotidacin, an investigational, first-in-class oral antibiotic with a novel mechanism of action for the treatment of female adults (≥40 kg) and adolescents (≥12 years, ≥40 kg) with uncomplicated urinary tract infections (uUTIs).

The FDA has granted Priority Review for this application and assigned a Prescription Drug User Fee Act (PDUFA) action date of March 26, 2025.

Over half of all women are affected by uUTIs in their lifetime,[1] with approximately 30% suffering from recurrent disease which can cause significant patient burden, including discomfort and restriction of daily activities.[2] New treatments are needed as the number of uUTIs caused by drug-resistant bacteria is increasing and can result in higher treatment failure rates.[3] Gepotidacin is a late-stage antibiotic in GSK's growing infectious disease portfolio and could be the first in a new class of oral antibiotics for uUTIs in over 20 years.

The NDA is supported by positive results from the pivotal phase III EAGLE-2 and EAGLE-3 trials. In these studies, gepotidacin demonstrated non-inferiority to nitrofurantoin, the current standard of care for uUTI, in female adults (≥40 kg) and adolescents (≥12 years, ≥40 kg) with a confirmed uUTI and a uropathogen susceptible to nitrofurantoin. In EAGLE-3, gepotidacin achieved statistically significant superiority versus nitrofurantoin, demonstrating therapeutic success in 58.5% (162/277) of participants compared to 43.6% (115/264) for nitrofurantoin (treatment difference 14.6%, 95% CI (6.4, 22.8)). In EAGLE-2, gepotidacin demonstrated therapeutic success in 50.6% (162/320) of participants compared to 47.0% (135/287) for nitrofurantoin (treatment difference 4.3%, 95% CI (-3.6, 12.1)).

The safety and tolerability profile of gepotidacin in the EAGLE-2 and EAGLE-3 phase III trials was consistent with previous trials of gepotidacin. The most commonly reported adverse events (AEs) in gepotidacin participants were gastrointestinal (GI). Diarrhoea was the most common (16% of participants), followed by nausea (9%). Of the participants who reported GI AEs in the gepotidacin group, the maximum severity were mild (69% Grade 1) and moderate (28% Grade 2). Participants with Grade 3 GI events accounted for 3% of all GI event cases and occurred in <1% of all participants. There was one drug-related serious adverse event in each treatment arm (gepotidacin and nitrofurantoin) across the two trials.

The development of gepotidacin has been funded in part with federal funds from the US Department of Health and

Human Services, Administration for Strategic Preparedness and Response, Biomedical Advanced Research and Development Authority (BARDA), under Other Transaction Agreement number HHSO100201300011C and with federal funds awarded by the Defense Threat Reduction Agency under agreement number HDTRA1-07-9-0002.

About the EAGLE (Efficacy of Antibacterial Gepotidacin Evaluated) phase III programme
The global phase III clinical programme for gepotidacin in adults and adolescents consists of three trials:

EAGLE-2 and EAGLE-3 (non-inferiority uUTI trials) compared the efficacy and safety of gepotidacin (1,500mg administered orally twice daily for five days) to nitrofurantoin (100mg administered orally twice daily for five days) with 1531 and 1605 female adults and adolescents with uncomplicated urinary tract infections, respectively. Across both trials, the duration of follow-up for participants was approximately 28 days, and the primary endpoint was the combined clinical and microbiological response at the Test-of-Cure (ToC) visit (days 10-13) in patients with qualifying uropathogens susceptible to nitrofurantoin.

EAGLE-1 (non-inferiority urogenital gonorrhoea trial) compared the efficacy and safety of gepotidacin to ceftriaxone plus azithromycin in 628 patients with uncomplicated urogenital gonorrhoea caused by *Neisseria gonorrhoeae*.

About gepotidacin
Gepotidacin, discovered by GSK scientists, is an investigational bactericidal, first-in-class triazaacenaphthylene antibiotic that inhibits bacterial DNA replication by a distinct binding site, a novel mechanism of action and for most pathogens, provides well-balanced inhibition of two different Type II topoisomerase enzymes. This provides activity against most target uropathogens (such as *E. coli* and *S. saprophyticus*), and *N. gonorrhoeae*, including isolates resistant to current antibiotics. Efficacy and safety in patients has been demonstrated in uUTI and gonorrhoeae phase III clinical trials, including those with drug-resistant pathogens. Due to the well-balanced inhibition, gepotidacin target-specific mutations in both enzymes are needed to significantly affect susceptibility to gepotidacin. Therefore, leading to a lower potential for resistance development.

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. GSK's expertise and capabilities in innovation, access and stewardship position the Company uniquely to help prevent and mitigate the challenge of antimicrobial resistance.

In antimicrobials, in addition to gepotidacin, GSK entered into an exclusive licence agreement with Spero Therapeutics, Inc. in September 2022 to add tebipenem HBr, a late-stage antibiotic and potential treatment for complicated urinary tract infections (cUTIs), to the pipeline and are currently enrolling for PIVOT-PO, a phase III trial. In March 2023, GSK announced an exclusive licence agreement with Scynexis for *Brexafemme* (ibrexafungerp tablets), a first-in-class antifungal for the treatment of vulvovaginal candidiasis (VVC) and reduction in the incidence of recurrent VVC.

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.

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Cautionary statement regarding forward-looking statements
GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described under Item 3.D "Risk factors" in GSK's Annual Report on Form 20-F for 2023, and GSK's Q2 Results for 2024.

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