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GSK announces positive headline results from EAGLE-1 phase III trial for gepotidacin in uncomplicated urogenital gonorrhoea (GC)

- EAGLE-1 trial met its primary efficacy endpoint of non-inferiority comparing gepotidacin with intramuscular ceftriaxone plus oral azithromycin combination therapy
- *Neisseria gonorrhoeae*, the bacteria causing gonorrhoea, is recognised by the World Health Organisation as a priority pathogen, for which resistance to existing treatments is rising
- Gepotidacin, a late-stage antibiotic in GSK's industry-leading infectious diseases portfolio, is also in development for uncomplicated urinary tract infections (uUTI)

GSK plc (LSE/NYSE: GSK) today announced positive headline results from the pivotal EAGLE-1 phase III trial for gepotidacin, a potential first-in-class oral antibiotic with a novel mechanism of action for uncomplicated urogenital gonorrhoea in adolescents and adults. The trial met its primary efficacy endpoint, with gepotidacin (oral, two doses of 3,000mg) demonstrating non-inferiority to intramuscular (IM) ceftriaxone (500mg) plus oral azithromycin (1,000mg), a leading combination treatment regimen for gonorrhoea. The result is based on a primary endpoint of microbiological response (success or failure) at the Test-of-Cure (ToC) visit 3-7 days after treatment.

Chris Corsico, Senior Vice President, Development, GSK, said: "With rising incidence rates and concern around growing resistance to existing treatments, gonorrhoea poses a threat to public health globally. These positive headline results demonstrate the potential for gepotidacin to provide a novel oral treatment option in the face of rising resistance and for patients who cannot take other treatments due to allergies or intolerance."

Gonorrhoea is a sexually transmitted infection caused by bacteria called *Neisseria gonorrhoeae*. It has been estimated that there are 82 million new cases globally each year.^[i] In the United States, rates of reported gonorrhoea have increased 118% from 2009 to 2021^[ii], with 648,056 cases being reported to the US Centers for Disease Control and Prevention (CDC) in 2022.^[iii] Gonorrhoea affects both men and women and if left untreated or inadequately treated, it can lead to infertility and other sexual and reproductive health complications. It also increases the risk of HIV infection.ⁱ

The safety and tolerability profile of gepotidacin in the EAGLE-1 phase III trial was consistent with results seen in gepotidacin phase I and II trials.

Detailed results from the EAGLE-1 trial will be presented at an upcoming scientific meeting and shared with global health authorities.

GSK is also developing gepotidacin for the potential treatment of uncomplicated urinary tract infections (uUTI). Positive phase III data from the EAGLE-2 and EAGLE-3 trials were presented at the European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) in Copenhagen in April 2023, and subsequently published in [The Lancet](#).^[iv] If approved, gepotidacin could be the first in a new class of oral antibiotics in uUTI in over 20 years.

The development of gepotidacin has been funded in whole or 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 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 has now been completed. The programme comprises of three trials:

EAGLE-1 (non-inferiority urogenital gonorrhoea trial) compared the efficacy and safety of gepotidacin to ceftriaxone plus azithromycin in approximately 600 patients with uncomplicated urogenital gonorrhoea caused by *Neisseria gonorrhoeae*.

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). Across both trials, the duration for participants was approximately 28 days, and the primary endpoint was the combined clinical and microbiological response at the ToC visit (days 10-13) in patients with qualifying uropathogens susceptible to nitrofurantoin.

About gepotidacin

Gepotidacin, discovered by GSK scientists, is an investigational bactericidal, first-in-class triazaacenaphthylene antibiotic that inhibits bacterial DNA replication by a novel mechanism of action and binding site and for most pathogens provides well-balanced inhibition of two different Type II topoisomerase enzymes. This provides activity against most strains of target uropathogens, (such as *E. coli* and *S. saprophyticus*), and *N. gonorrhoeae*, including isolates resistant to current antibiotics. Due to the well-balanced inhibition of two enzymes, gepotidacin target-specific mutations in both enzymes are needed to affect susceptibility to gepotidacin significantly.

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. 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 (cUTI), to the pipeline. 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](https://www.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 the company's Annual Report on Form 20-F for 2022, and Q4 Results for 2023.

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[i] World Health Organisation, Multi-drug resistant gonorrhoea. Available at: <https://www.who.int/news-room/fact-sheets/detail/multi-drug-resistant-gonorrhoea>

[ii] CDC data on file

[iii] CDC Sexually Transmitted Infections Surveillance, 2022, available at:

<https://www.cdc.gov/std/statistics/2022/default.htm#:~:text=In%202022%2C%20more%20than%202.5,from%20all%20STI%20prevention%20partners>

[iv] The Lancet, Oral gepotidacin versus nitrofurantoin in patients with uncomplicated urinary tract infection (EAGLE-2 and EAGLE-3): two randomised, controlled, double-blind, double-dummy, phase 3, non-inferiority trials, available at:

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(23\)02196-7/abstract](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)02196-7/abstract)



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