GSK announces positive Phase IIa study results for a new first-in-class candidate medicine for patients with tuberculosis

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For media and investors only

- GSK3036656 demonstrated early bactericidal activity with a low, once-daily oral dose after 14 days of treatment in participants with drug-susceptible pulmonary tuberculosis

- Treatment was generally well tolerated with no serious adverse events identified

- Results demonstrate the potential for this asset to be a component of simpler TB treatment regimens in the future

- TB remains leading global cause of death from infectious disease and new treatments are urgently needed

GSK plc (LSE/NYSE: GSK) today announced positive results from a Phase IIa study demonstrating that GSK3036656, a first-in-class investigational antitubercular agent, was well tolerated and showed early bactericidal activity with a low, once-daily oral dose after 14 days of treatment in participants with drug-susceptible pulmonary tuberculosis. These results demonstrate the potential for GSK3036656 to be a component of simpler treatment regimens in the future which could help address the TB epidemic.

A selection of these data was presented in an oral late breaker session at the Union World Conference on Lung Health on 11 November. The TB epidemic is one of the most pressing public health challenges: over the last decade TB was the leading cause of death due to an infectious disease globally, causing approximately 1.5 million deaths annually. Earlier this year, GSK made a commitment to invest £1bn over the next decade to accelerate R&D on infectious

diseases, including TB, that disproportionately impact lower-income countries.

David Barros-Aguirre, Head of Global Health Medicines R&D, GSK, said:

> Existing treatments for TB can be complicated, of long duration and have serious side effects which significantly impact the lives of patients with TB around the world. Today's encouraging data provide a good foundation from which to investigate GSK3036656 in different combinations in Phase IIb/c studies, with the aim of contributing to shorter, simpler and better tolerated treatment regimens for patients with TB.

Anti-mycobacterial activity was demonstrated both in terms of reducing the number of viable TB cells which are able to multiply (colony forming units - CFU), and an increase in the time to detect bacterial growth in culture (time to positivity - TTP). In addition, PET CT imaging of the lungs showed a reduction in TB disease over 14 days in all participants taking GSK3036656 30mg.

Prof. Andreas Diacon, Chief Scientific Officer, TASK, said

> The data show that GSK3036656 is a potential new antibiotic for tuberculosis that can be used in low, once daily doses. This can help reduce side effects and is an important characteristic of any new TB drug. GSK3036656 is of a completely new class of antibiotics which makes the chance of drug resistance very low. I am looking forward to evaluating GSK3036656 in shorter and better tolerated combinations with other new agents to bring about a new era of tuberculosis treatment.

The investigational antitubercular agent will be tested in Phase IIb/c studies in different drug regimens to determine the appropriate partner agents to complement its anti-TB action and the optimal regimen durations. The aim is to identify a GSK3036656-containing regimen with sufficient tolerability, efficacy and short enough duration to progress to Phase III with a high probability of success. These innovative studies will be conducted in collaboration with industry and academic partners and will be co-funded by the European Union's IMI2 programme.

GSK works in partnership to develop new TB medicines and vaccines,

focusing efforts on research and early development, and partnering with world-leading organisations and funders on late development, manufacturing and access to maximise impact for patients.

Study 201214 was a single centre, Phase IIa, open-label study to investigate the early bactericidal activity (EBA), safety, and tolerability of GSK3036656 in participants with drug-sensitive pulmonary tuberculosis. The study had four cohorts, with 12 to 20 participants in each cohort. The participants were randomized in a 3:1 ratio to receive either GSK3036656 at doses 1 mg, 5 mg, 15 mg, and 30 mg or standard-of-care (SoC) regimen for drug sensitive TB (i.e. Rifafour e-275 or equivalent generic alternative), respectively.

The primary endpoint was to determine the rate of change in log10colony forming units (CFU) per mL direct respiratory sputum samples over the period baseline to Day 14 (EBA CFU0-14). A key secondary outcome was the rate of change in time to sputum culture positivity (EBA TTP) over the time period baseline to Day 14 (EBA TTP0-14).

GSK3036656 doses of 5 mg to 30 mg showed bactericidal activity as evidenced by both endpoints after 14 days. GSK3036656 30 mg had the highest bactericidal activity:

- A decline in CFU of -0.138 log10CFU/mL (95% CI: -0.167, -0.109)

- An increase in TTP of 0.22 log10CFU/mL (95% CI: 0.019, 0.024)

GSK3036656 was generally well tolerated with no serious adverse events (SAEs) identified in the study. The percentage of participants reported with adverse events was similar between SoC and GSK3036656 and no large differences between GSK3036656 and SoC or GSK3036656 dose related trends were observed.

The trial was conducted as part of the anTBiotic project, a consortium which consists of GSK Global Health Medicines R&D (Spain), the University of Tromsø (Norway), Forschungszentrum Borstel (Germany), the University of Cape Town (South Africa) and the TASK Foundation (South Africa). The project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 733079.

Tuberculosis is the leading cause of death due to an infectious

disease globally, other than COVID-19, causing approximately 1.5 million deaths annually. It is caused by a bacterium called Mycobacterium tuberculosis and mainly affects the lungs, although it can affect any part of the body.

Current treatment options are often inadequate for patients with TB: long and complicated courses of treatment with serious side effects mean many people struggle to adhere to the full course. As a result, the bacteria are developing resistance to existing medicines making treatment less effective. New treatments are urgently needed: the ambition is to find shorter, simpler and better tolerated treatments for TB to reduce the burden on patients and increase adherence to treatment thereby preventing further selection of resistant strains.

However, developing new TB treatment regimens is challenging as they involve a combination of more than three different compounds often from multiple organisations. A collaborative approach is required to ensure researchers can access the compounds at an early stage of development to understand how they work in combination.

GSK3036656 is a first-in-class investigational antitubercular agent which is being developed for the treatment of tuberculosis as part of a future combination regimen. It suppresses protein synthesis in Mycobacterium tuberculosis (Mtb) by inhibiting the enzyme leucyl t-RNA synthetase (LeuRS).

GSK3036656 has demonstrated activity not only against laboratory strains of Mtb, but also against a selection of Drug Sensitive TB (DS-TB), Multi Drug Resistant TB (MDR-TB) and Extensively Drug Resistant TB (XDR-TB) clinical isolates. Animal models of TB infection have shown that GSK3036656 is potent in vivo.

The compound is the result of a collaboration between GSK and Anacor Pharmaceuticals which led to the identification of GSK3036656 as a selective anti-mycobacterial agent that is inactive against other respiratory pathogens.

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/company

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 in the Company's Annual Report on Form 20-F for 2021, GSK's Q3 Results for 2022 and any impacts of the COVID-19 pandemic.

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