PRESS RELEASE

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GSK candidate vaccine demonstrates sustained level of protection against active pulmonary tuberculosis

- Final analysis of phase IIb study published today in the New England Journal of Medicine and presented at the 50th Union World Conference on Lung Health.
- Final results confirm the innovative TB candidate vaccine's efficacy level and acceptable safety profile in three-year clinical trial conducted in sub-Saharan African regions.

Today, GSK and IAVI reported that GSK's M72/AS01E[1] candidate vaccine significantly reduced the incidence of pulmonary tuberculosis disease (TB) in HIV-negative adults with latent TB infection[2]. These results demonstrate an overall vaccine efficacy of 50% during the three years after vaccination. The candidate vaccine has an acceptable safety and reactogenicity profile. The final results are consistent with the primary analysis done after two years of follow-up and published in *New England Journal of Medicine* in September 2018.

TB is the leading cause of death through infectious disease worldwide and represents a significant public health threat with 1.5 million attributed deaths in 2018[3]. It is estimated that one-quarter of the global population has latent TB infection, of whom approximately 10% will develop active pulmonary TB disease. Currently, multi-drug resistant strains of TB are emerging and spreading globally, and the only available TB vaccine, BCG, does not provide proven and consistent protection in adults in TB-endemic countries[4]. Without a more effective vaccine, it will not be possible to achieve the World Health Organization target of decreasing the number of new cases by 90% and the number of TB deaths by 95% between 2015 and 2035.

Dr Thomas Breuer, Chief Medical Officer of GSK Vaccines, said: "*These results demonstrate that for the first time in almost a century, the global community potentially has a new tool to help provide protection against TB. I want to thank our scientists for their dedicated effort and scientific innovation in developing this impactful vaccine candidate in partnership with IAVI and other key organisations.*"

The trial was conducted in TB-endemic regions (Kenya, South Africa and Zambia) and involved 3,573 HIV-negative adults between the ages of 18 and 50 years. Participants who received two doses of either M72/AS01E or placebo 30 days apart were followed for three years to detect evidence of pulmonary tuberculosis disease. In the final analysis, 13 participants in the vaccine group developed active pulmonary tuberculosis compared to 26 participants in the placebo group. Among participants who received the vaccine, an increased M72-specific immune response was sustained through three years.

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[1] The GSK proprietary AS01 adjuvant system contains QS-21 Stimulon® adjuvant licensed from Antigenics LLC, a wholly owned subsidiary of Agenus Inc. (NASDAQ: AGEN), MPL and liposomes

[2] WHO, Latent tuberculosis infection: updated and consolidated guidelines for programmatic management, 2018

[3] WHO, Global Tuberculosis Report, 2019

[4] WHO, Weekly Epidemiological Record, 23 February 2019, vol.93 (pp73-96) : BCG vaccines, WHO position paper

Dr. Mark Feinberg, President and CEO of IAVI, said: "*These final results show that M72/AS01$_E$ could be an important tool in the fight against pulmonary tuberculosis. While additional trials need to be conducted to confirm these findings in other populations, we have never before seen a vaccine that provides protection in adults who are already infected with the bacteria that cause tuberculosis*."

About the study

The study was sponsored by GSK and conducted in partnership with IAVI. Funders of IAVI for this study were the Bill & Melinda Gates Foundation, the United Kingdom's Department for International Development, the Directorate General for International Cooperation in the Netherlands, and the Australian Agency for International Development.

This study was a phase IIb, multicentre, randomized, double-blind, placebo-controlled study comparing the candidate vaccine M72/AS01$_E$ to a placebo in a 1:1 ratio. It was conducted in tuberculosis-endemic regions, at 11 sites in Kenya, South Africa and Zambia[5] (www.clinicaltrials.gov NCT01755598). The primary objective of the study was to investigate if the M72/AS01$_E$ candidate vaccine prevents adults with latent *Mycobacterium tuberculosis* infection from developing pulmonary tuberculosis disease. The study also evaluated the safety, reactogenicity and immunogenicity of the M72/AS01$_E$ candidate vaccine.

The primary results of this study were published in September 2018 in the *New England Journal of Medicine* (DOI: NEJMdo005415). The primary analysis was performed while the study team remained blinded to individual trial group assignment, whereas the final analysis was now performed under fully unblinded conditions. The study's final results confirmed the previously reported clinically acceptable safety profile of M72/AS01$_E$. No patterns were evident in the extended follow-up in terms of occurrence or nature of serious adverse events, fatal events or potential immune-mediated diseases over the study period.

Nearly all participants (99%) in the study consented to enter into a biobanking study sponsored by IAVI. The samples collected during this study will allow researchers to further investigate the potential vaccine-induced mechanisms of protection against tuberculosis and attempt to identify markers that indicate those who are protected by vaccine (www.clinicaltrials.gov NCT02097095).

About the candidate vaccine

GSK's M72/AS01$_E$ candidate vaccine contains the M72 recombinant fusion protein, derived from two *Mycobacterium tuberculosis* antigens (Mtb32A and Mtb39A), combined with the Adjuvant System AS01, which is also a component of GSK's RTS,S malaria vaccine and vaccine against shingles, *Shingrix*.

About tuberculosis

One-quarter of the global population is estimated to have latent tuberculosis infection, and tuberculosis is the leading infectious cause of death worldwide. There were an estimated 10 million new tuberculosis cases and 1.5 million deaths attributed to tuberculosis in 2018[6,7]. Pulmonary tuberculosis, which involves the lung, is responsible for the spread of the disease from person-to-person. An effective vaccine against tuberculosis administered in adolescents and adults would have a marked impact on tuberculosis control, including drug-resistant tuberculosis, through interruption of

[5] Sites in South Africa: SATVI, Task, Setshaba, Aurum-Klerksdorp, Aurum-Tembisa, PHRU, CIDRI, and Be Part; sites in Zambia: CIDRZ and Zambart; and site in Kenya: KEMRI.

[6] Houben RM, Dodd PJ. The Global Burden of Latent Tuberculosis Infection: A Reestimation Using Mathematical Modelling. PLoS Med 2016;13:e1002152

[7] WHO. Global Tuberculosis Report, 2019

transmission[8,9], and it would help achieve the WHO target of ending the tuberculosis epidemic by 2035.

About IAVI

IAVI is a nonprofit scientific research organization dedicated to addressing urgent, unmet global health challenges including HIV and tuberculosis. Our mission is to translate scientific discoveries into affordable, globally accessible public health solutions. Read more at iavi.org.

IAVI enquiries:

Africa enquiries:	Ethel Makila	+254 71 904 3142	EMakila@iavi.org
Europe enquiries:	Hester Kuipers	+31 20 521 0343	HKuipers@iavi.org
India enquiries:	Saif ul Hadi	+91 11 4737 6032	SulHadi@iavi.org
United States enquiries:	Rose Catlos	+1 212 847 1049	RCatlos@iavi.org

About GSK

GSK is a science-led global healthcare company with a special purpose: to help people do more, feel better, live longer. For further information please visit www.gsk.com.

GSK enquiries:

UK Media enquiries:	Simon Moore	+44 (0) 20 8047 5502	(London)
US Media enquiries:	Evan Berland	+1 215 751 5497	(Philadelphia)
Analyst/Investor enquiries:	Sarah Elton-Farr	+44 (0) 208 047 5194	(London)
	Danielle Smith	+44 (0) 20 8047 7562	(London)
	James Dodwell	+44 (0) 20 8047 2406	(London)
	Jeff McLaughlin	+1 215 751 7002	(Philadelphia)

[8] Dheda K, Gumbo T, Maartens G, et al. The epidemiology, pathogenesis, transmission, diagnosis, and management of multidrug-resistant, extensively drug-resistant, and incurable tuberculosis. Lancet Respir Med 2017; 5:291-360

[9] Harris RC, Sumner T, Knight GM, White RG. Systematic review of mathematical models exploring the epidemiological impact of future TB vaccines. Hum Vaccin Immunother 2016;12:2813-32