TBCAB GLOBAL TB COMMUNITY ADVISORY BOARD

TAG Treatment Action Group

5 April 2019

Statement by the Global TB Community Advisory Board to the High-Level Consultation on Accelerating the Development of the M72/AS01$_E$ Tuberculosis Vaccine Candidate

The Global TB Community Advisory Board (Global TB CAB) wishes to submit the following statement to the *High-level consultation on accelerating the development of the M72/AS01$_E$ tuberculosis vaccine candidate* convened by the World Health Organization (WHO) on April 5, 2019.

The Global TB CAB is a group of research-literate, community-based activists from HIV and tuberculosis (TB) networks across the world. Founded in 2011 and hosted by Treatment Action Group (TAG), the TB CAB is dedicated to increasing meaningful community engagement in TB research and to mobilizing political will to advance the development and uptake of new tools to fight TB. We act in an advisory capacity to product developers and institutions conducting clinical trials of new TB drugs, drug regimens, diagnostics, and vaccines.

We write to you from Bangkok, Thailand, where our group has convened with other members of civil society to strategize about advocacy to accelerate TB innovation. Advancing TB research is an urgent scientific, public health, and human rights priority for our communities, and the development of a new TB vaccine is a critical piece of the TB research agenda.

In this spirit, we wish to congratulate GlaxoSmithKline Biologicals (GSK) on the positive results from the phase IIb trial of TB vaccine candidate M72/AS01$_E$ published in the New England Journal of Medicine (NEJM) in September 2018. The finding that vaccination with M72/AS01$_E$ provided 54.0% protection to HIV-negative adults with TB infection from developing active TB disease is a signal of extraordinary promise. We understand that this represents a prespecified primary analysis conducted after participants completed at least two years of follow-up, and that this positive efficacy signal must be confirmed by a final analysis after three years of follow-up, which has yet to be reported. It is our hope that if this signal is confirmed, GSK will commit to urgently advancing this promising vaccine candidate into a phase III clinical trial.

As WHO convenes GSK and other important stakeholders in Geneva for this high-level consultation on accelerating the development of M72/AS01$_E$, we wish to deliver the following messages from the TB-affected communities we represent:

1. **Prepare for success by initiating planning for a phase III trial now**. United Nations member states have embraced the ambitious goal of ending TB by 2030, as reflected in the Sustainable Development Goals and reinforced by the political declaration of the UN High-Level Meeting on TB. We will not end TB without equal ambition in research, and that requires adopting a mindset that embraces risk and plans for success. We understand that final analyses from the M72/AS01$_E$ phase IIb study could be shared as early as October 2019. In the interim, we encourage GSK, WHO, public funders, and other stakeholders to start devising plans for a phase III trial so as to make efficient use of time and to capitalize on the political will generated by the UN High-Level Meeting on TB last year.

2. **Ensure the design of any phase III study supports future research endeavors**. One strength of the M72/AS01$_E$ phase IIb trial was its inclusion of a biobank to which 99% of trial participants consented to contributing blood samples pre- and post-vaccination. This biobank will enable researchers to search for immune correlates of protection and support other basic

and translational science objectives. We consider biobanking to be an ethical imperative of any phase III study, since this will help ensure the social and scientific value of any future trial, regardless of study outcomes.

3. **Ensure that any phase III trial informs both licensure and policymaking**. A phase III trial should do more than satisfy stringent regulatory requirements. Its design should also support the production of clear normative guidance from WHO to enable quick, confident adoption by national health systems. A critical piece of this is the inclusion of people living with HIV (PLHIV) in the trial. This could be accomplished by enrolling a cohort of PLHIV to be evaluated for safety and immunogenicity endpoints. We also believe that the threshold for adolescent inclusion in TB vaccine studies should be broadened to include those aged 12 years and older, for both epidemiologic and biological reasons. Excluding PLHIV and adolescents from a phase III trial would mean that two of the groups that face the highest risk of TB would be precluded from enjoying the direct benefits of a new TB vaccine.

4. **Consult with TB-affected communities and civil society early and often in preparing for a phase III trial**. The meaningful participation of communities in TB research is a core element of "good participatory practice (GPP)," as outlined in the *Good Participatory Practice Guidelines for TB Vaccine Research* and in the WHO *Ethics Guidance for the Implementation of the End TB Strategy*. GPP requires that community representatives have a voice at each step of the research process, from the design of studies to trial implementation to the translation of results into policy and practice. This participation often starts with community review of study concepts and protocols, and we encourage GSK and any involved partners to engage our group and other TB community groups on questions relating to study design, study populations, geographic representation, sub-analyses/secondary endpoints, inclusion of special populations (e.g., PLHIV, adolescents, children), biobanking, and informed consent.

5. **Commit to equitable, affordable access to M72/AS01$_E$ should a phase III trial confirm its safety and efficacy**. Given the likelihood that a phase III trial will involve unprecedented levels of public funding from many governments, as well as philanthropic dollars, it is imperative that the final product be treated as a true global public good and made equitably available to all who may benefit from it. This is in keeping with the commitment by UN member states in the TB political declaration to approach TB research and development "as a shared responsibility…aiming to be needs-driven, evidence-based, and guided by the principles of affordability, effectiveness, efficiency, and equity." At a minimum, this should include: 1) setting a single global access price for M72/AS01$_E$, and 2) registering the vaccine widely with national regulatory authorities.

6. **Take steps to ensure a sufficient, stable supply of M72/AS01$_E$ following a successful phase III trial**. We have heard concerns about supply constraints affecting the AS01$_E$ adjuvant system, in particular regarding one of its components (QS-21). At the same time, we understand that M72/AS01$_E$ employs the same adjuvant system as that used in two licensed GSK vaccines: Mosquirix™ and Shingrix™, the latter of which uses AS01B (double the dose of AS01E). Persistent shortages of Shingrix™ lead us to worry that manufacturing constraints may negatively affect timelines for a phase III trial**.** We encourage GSK to consider partnering with developing country vaccine manufacturers from the outset of a phase III trial to ensure that supply constraints are not a barrier. This could involve licensing the AS01$_E$ adjuvant system to a qualified generic manufacturer for a TB indication via technology transfer, or through the use of mechanisms such as the Medicines Patent Pool.