Nota MTBVAC WHO END-TB 15 July 2025

**MTBVAC candidate vaccine**

MTBVAC is an attenuated *Mycobacterium tuberculosis* vaccine candidate developed to provide improved protection over BCG in both infants and adults. It is the only TB vaccine in clinical development derived from a human isolate of *M. tuberculosis*. MTBVAC is an attenuated by genetically engineering two independent unmarked stable deletion in the virulence genes *phoP* and *fadD26*, based on clinical strain of the Euro-American lineage 4, the most widespread transmitted lineage between humans (Arbues *et al* Vaccine 2013).

Importantly, MTBVAC includes the RD1 region – deleted in BCG- , which contains approximately 23% of the known human T-cell epitopes of *M. tuberculosis*, potentially broadening its immunogenic (Aguilo *et al* Nat Comm 2017). In preclinical studies, MTBVAC has shown superior protection compared to BCG in mice, guinea pigs, and non-human primates. In particular, studies in macaques using adult-relevant protocols (same intradermal dose and aerosol *M. tuberculosis* challenge) confirmed enhanced efficacy in preventing infection and disease (White *et al* 2021 npg Vaccines).

**Development and partnerships**

BIOFABRI S.L.U., is a Spanish biopharmaceutical company belonging to the European biopharmaceutical group ZENDAL HEALTH. Biofabri leads the development, manufacture and global marketing of MTBVAC and is the Sponsor of the phase III trial in newborns. Key partners in the MTBVAC programme include:,

- The University of Zaragoza (UNIZAR, Spain), intellectual owner of MTBVAC.
- The European non-profit Tuberculosis Vaccine Initiative (TBVI) (www.tbvi.eu) (Lelystad, The Netherlands), who supports clinical and regulatory development in newborns
- IAVI (www.iavi.org) (New York, USA), sponsor of the Phase 2b trial in sub-Saharan Africa. Provides support in clinical and regulatory development and leads global access activities in adolescent and adults
- Bharat Biotech (BBIL) (Hyderabad, India), sponsor of all clinical trials in India, leads regulatory, manufacturing, commercialization, and distribution activities in 70 countries of Africa and South-East Asia.
- Ataulpho de Paiva Foundation (FAP) (Rio de Janeiro, Brazil), leads clinical development in Brazil, and all regulatory, manufacturing, commercialization, and distribution activities in 35 countries of Latin American.

**Regulatory status**

MTBVAC received early access to PRIME scheme programme by EMA in 2018 and simultaneously was considered eligible for Art. 58 procedure (EU-M4All).

In January 2024 full access to PRIME was granted.

**Clinical Development**

MTBVAC has completed Phase 1 Clinical trials in adults in Europe (Spertini *et al* Lancet Respir Med 2012) and newborns in Africa (Tameris *et al* Lancet Respir Med 2019), demonstrating a favorable safety profile and robust immunogenicity. A recently completed Phase 2 trial in South Africa assessed MTBVAC in adults with and without latent TB infection to define the optimal dose and guide future efficacy trials in adolescents and adults—the populations driving TB transmission (Luabeya *et al* Lancet Global Health 2025). Additional trials have also been conducted in newborns (Tameris *et al* Ebiomedicine 2025).

MTBVAC is currently in Phase 3 clinical development (Stop TB Partnership). A pivotal efficacy trial in newborns is underway in South Africa, with over 4000 neonates already vaccinated (NCT04975178). In parallel, a Phase 2b study in adolescents and adults is ongoing in South Africa, Kenya and Tanzania (NCT06272812). Additionally, a dedicated study in HIV positive individuals is being conducted in South Africa (NCT05947890).

In 2024, BBIL, in collaboration with Biofabri, initiated a series of clinical trials in India to evaluate the safety, immunogenicity, and efficacy of MTBVAC. A Phase 2 trial is currently underway, with a pivotal trial assessing safety, immunogenicity, and efficacy planned to begin in 2025.

As a novel, live vaccine candidate with broad immune activation and strong preclinical and clinical performance, MTBVAC represents a complementary tool in the global TB vaccine pipeline.