BIOFABRI

Biotechnology and vaccines

MTBVAC for the prevention of TB disease

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THE PARTNERS

Biofabri: owner of MTBVAC (THE VACCINE), oversight and coordination of global development, sponsor of the phase 3 trial among infants. Leads all regulatory, manufacturing, commercialization, and distribution activities in 85 countries across America, Europe, Middle East, Oceania, and Asia

UNIZAR: MTBVAC-01 (The strain) was developed and preclinically studied by the University of Zaragoza. UNIZAR provides Scientific Advice to partners in clinical development

TBVI: development partner focused on activities leading to an infant indication for MTBVAC. Provides support to partners in the areas of clinical development and regulatory

IAVI: development partner focused on activities leading to an adult and adolescent indication. Sponsor of the phase 2b trial in sub–Saharan Africa. Provides support in the areas of CMC, clinical development, regulatory and global access planning activities

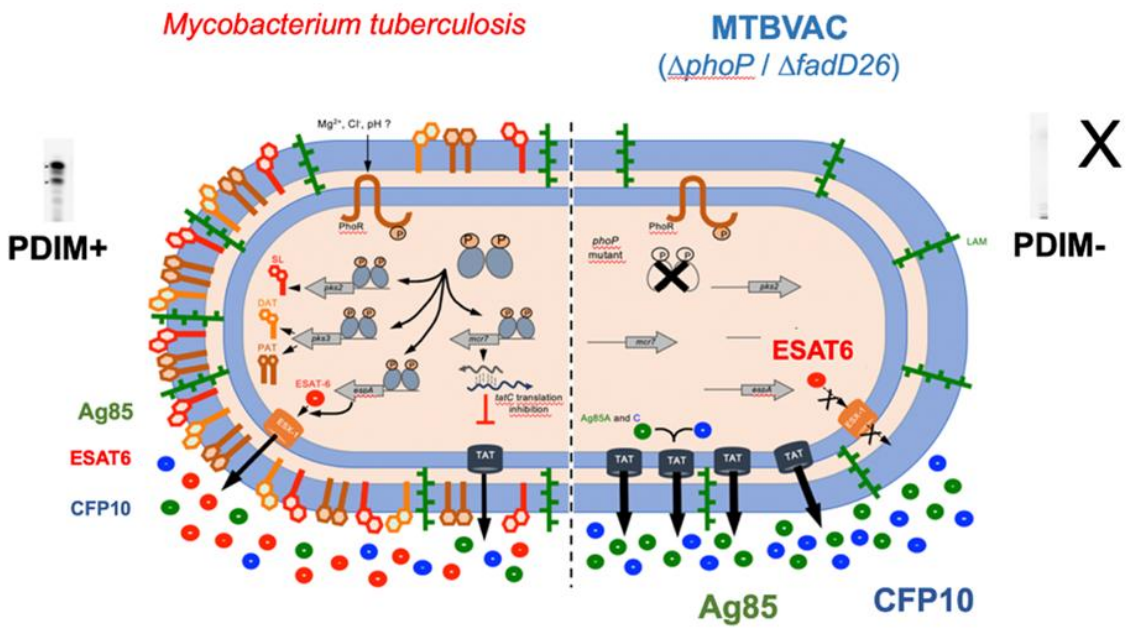
Bharat Biotech: sponsor of all clinical trials in India, leads all regulatory, manufacturing, commercialization, and distribution activities in 56 countries in Africa and in 25 countries in South-East Asia

FAP: Partner for clinical development and manufacturing in Brazil, and all regulatory, commercialization, and distribution activities in 34 Latin American countries

THE VACCINE CANDIDATE: MTBVAC

MTBVAC is being developed as a new intradermal TB vaccine for newborns, adolescents, and adults

- Only live-attenuated vaccine in development, derived from human *Mycobacterium tuberculosis*, not bovine tuberculosis (as BCG)
- Rationally attenuated by stable deletion of the two virulence genes *phoP* and *fadD26*, without antibiotic resistance markers
- Presents a wider collection of antigens of the original pathogen to the host immune system (including ESAT6 and CFP10, present in RD1 region)
- Through Pre-Clinical and Clinical evaluation has show increased immunogenicity and is designed to offer improved protection compared to BCG



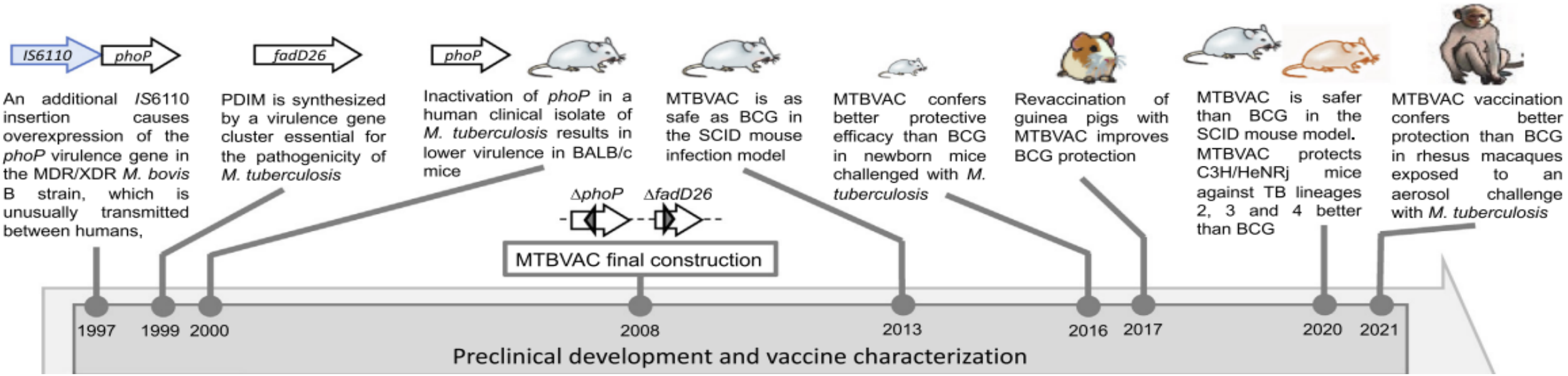
Deletion of *phoP* : loss of lipids **SL, PAT, DAT**; no secretion of **ESAT6**; increase in secretion of **MTB Ag 85 Complex**
Deletion of *fadD26* : loss of virulence factor **PDIM**

PRE-CLINICAL DEVELOPMENT

MTBVAC displayed a robust safety, biodistribution and persistence profile, comparable to BCG in GLP and non GLP studies

MTBVAC showed the ability to induce improved protective efficacy as compared to BCG both as priming and as boosting candidate (mice, GP and macaques)

The European Medicines Agency (EMA) has indicated that the preclinical data package is robust enough to be part of a licensure application for MTBVAC



Martín C, Marinova D, Aguiló N, Gonzalo-Asensio J. MTBVAC, a live TB vaccine poised to initiate efficacy trials 100 years after BCG. Vaccine. 2021 Dec 8;39(50):7277-7285. doi: 10.1016/j.vaccine.2021.06.049. Epub 2021 Jul 6. PMID: 34238608.

TARGET PRODUCT PROFILE

BIOFABRI

Efficacy and indication

- Relative efficacy for infants compared to BCG: 50% in the prevention of TB disease
- Efficacy for A/A compared to placebo: 50% in the prevention of active pulmonary TB disease

Duration of protection

- At least 5 years among infants
- At least 2 years among A/A

- One intradermal dose
- Lyophilized formulation
- Presentation in a multidose vial

NEWBORNS

Attribute	Upside Target	Minimally Acceptable Target
Indication for use	Prevention of TB disease	
Target population	All newborns	HIV-non-infected newborns
Relative efficacy (compared to BCG)	75%	50%
Duration of protection	≥10 years	≥ 5 years
Route of administration	Intradermal (ID)	
Schedule of administration	One dose	
Safety / reactogenicity	Improved reactogenicity and safety to BCG	Similar reactogenicity and safety to BCG
Use in special populations	Use in HIV infected individuals	HIV-non-infected newborns
Formulation	Lyophilized powder to be reconstituted with commercially available water-for-injections (WFI)	
Presentation	Multidose vial – no preservative 20-dose (2,5 x 10^5 CFU MTBVAC in 0.05 mL) Type I amber glass vials, closed with rubber stopper and aluminium seal	
Storage requirements Stability	24 months at +2ºC to +8ºC (storage conditions) Up to 8 hours at room temperature after reconstitution	12 months at +2 ºC to +8 ºC (storage conditions) Up to 4 hours at room temperature after reconstitution

ADULTS & ADOLESCENTS

Attribute	Upside Target	Minimally Acceptable Target
Indication for use	Prevention of active pulmonary TB disease	
Target population	Adolescents and adults	
Efficacy (compared to placebo)	VE≥ 50%	
Duration of protection	≥ 10 years	≥ 2 years
Route of administration	Intradermal (ID)	
Schedule of administration	One dose	
Safety / reactogenicity	Favourable Similar reactogenicity and safety profile compared to other vaccines recommended in this age group	
Use in special populations	Use in HIV infected individuals	Use in HIV infected individuals on ART and absence of clinical signs or symptoms of moderate or severe immunosuppression
Formulation	Lyophilized powder to be reconstituted with commercially available water-for-injections (WFI)	
Presentation	Multidose vial – no preservative 10-dose (5 x 10^5 CFU MTBVAC in 0.1 mL) Type I amber glass vials, closed with rubber stopper and aluminium seal	
Storage requirements Stability	24 months at +2ºC to +8ºC (storage conditions) Up to 8 hours at room temperature after reconstitution	12 months at +2 ºC to +8 ºC (storage conditions) Up to 4 hours at room temperature after reconstitution

PARTNERS ARE INVOLVED IN CLINICAL DEVELOPMENT

Completed
Ongoing
Planned

Phase 1a
36 QFT- (adults)
3 doses

Switzerland

Phase 1b
18 QFT- (adults)
36 neonates
1 dose

South Africa

Phase 1b/2a
72 QFT- (adults)
72 QFT+ (adults)
4 doses

South Africa

Phase 2a
99 neonates
3 doses

Phase 3
7120 neonates

Senegal
South Africa
Madagascar

Phase 2a
276 (84 HIV- /192 HIV+)
QFT+ and QFT- (adults)

South Africa

Phase 2b
4300 QFT + (adolescents and adults)
1200 QFT- (adolescents and adults)

Kenya
Tanzania
South Africa

Phase1
30 QFT- (adults)

Phase 2
82 QFT-/82 QFT+ (adults)

Phase 3
QFT-/QFT+ (adolescents and adults), under development

India

MOU Signed with FAP/FIOCRUZ and Upcoming engagements with ANVISA

Brazil

Phase 1 and 2 safety, immunogenicity and dose finding studies in neonates and adults in Europe and SSA show that MTBVAC is as **safe as and more immunogenic than BCG in QFT+ and QTF-.** The Phase 2 studies have allowed **selection of dose**

2012 2015 2019 2023 2024 2025 2030

HVTN 605/A5421: Phase 2a study in A&A living with HIV in RSA

Phase 2a clinical trial to evaluate the safety and immunogenicity of MTBVAC in adolescents and adults living with and without HIV in South Africa [NCT05947890]

Trial duration: 2024-2027

Sample size	N= 276 (QFT+ and QFT-); 12-55 years at 16 CRCs in SA
Control arm	Active control, BCG
Follow up duration	1 year
Cohorts	Part A (Cohort 1 and 2) 1) HIV- (N=84) 2) HIV+, CD4 T-cell count ≥ 200 cells/mm^3 (N=108) Part B (Cohort 3) 1) HIV+, CD4 T-cell count ≥ 100 cells/mm^3 (N=84)

Status: ongoing

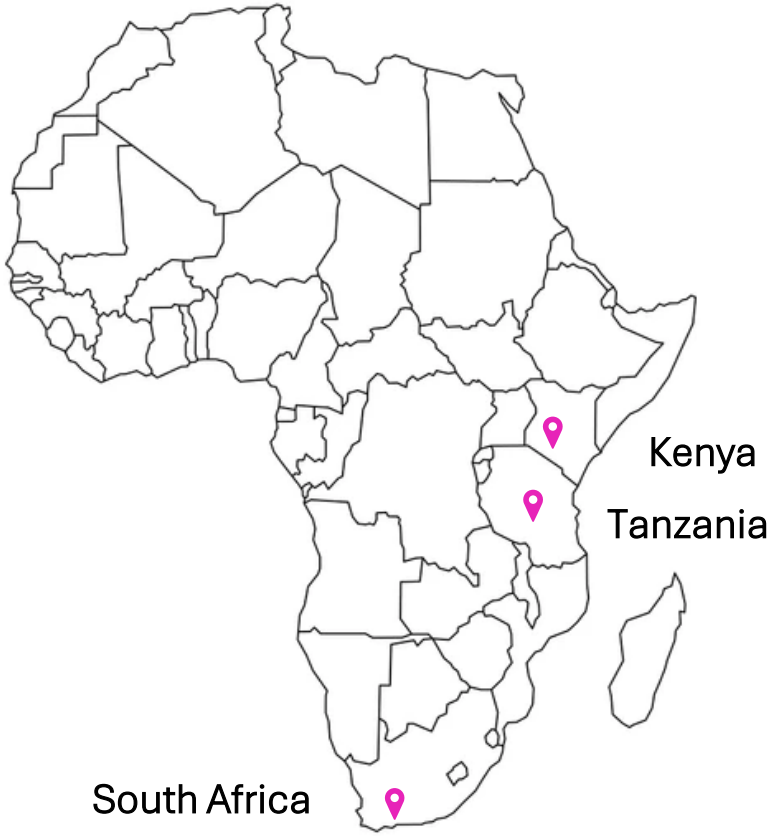
- 186 participants enrolled as of Apr 2026
- Resume enrolment in Q2 2026, end date expected by Q2 2027

IAVI C113 IMAGINE: Phase 2b study in A&A in SSA

Phase 2b safety and proof-of-concept (POC) efficacy study for prevention of TB disease in IGRA+ African adults and adolescents [NCT06272812]

Trial duration: 2025-2028

Sample size	N = 4,300 IGRA+; 14-45 years at 16 CRCs (13 in SA, 2 in KE, 1 in TZ)
Control arm	Placebo, randomized 1:1 double blind
Follow up duration	24-36 months
Primary endpoint	PTB diagnosed with at least 2 positive diagnostic tests (PCR and mycobacterial culture)*
Secondary endpoints	Efficacy (alternative case definitions), safety, immunogenicity
Exploratory endpoint	Subclinical (asymptomatic) TB, correlates of immune protection
Additional cohort	IGRA- for safety and immunogenicity N=1,200, 3:1 randomization



Status: Ongoing

- 3559 participants enrolled, as of 06/04/2026

*75% power; LB 95% CI ≥0

**Identical to sensitivity analysis for primary endpoint in the M72:AS01E phase 2b study and the primary endpoint for the M72:AS01E phase 3 study ((3 sputum samples obtained in 1 week if TB symptoms reported; each sent for PCR and Mtb culture)

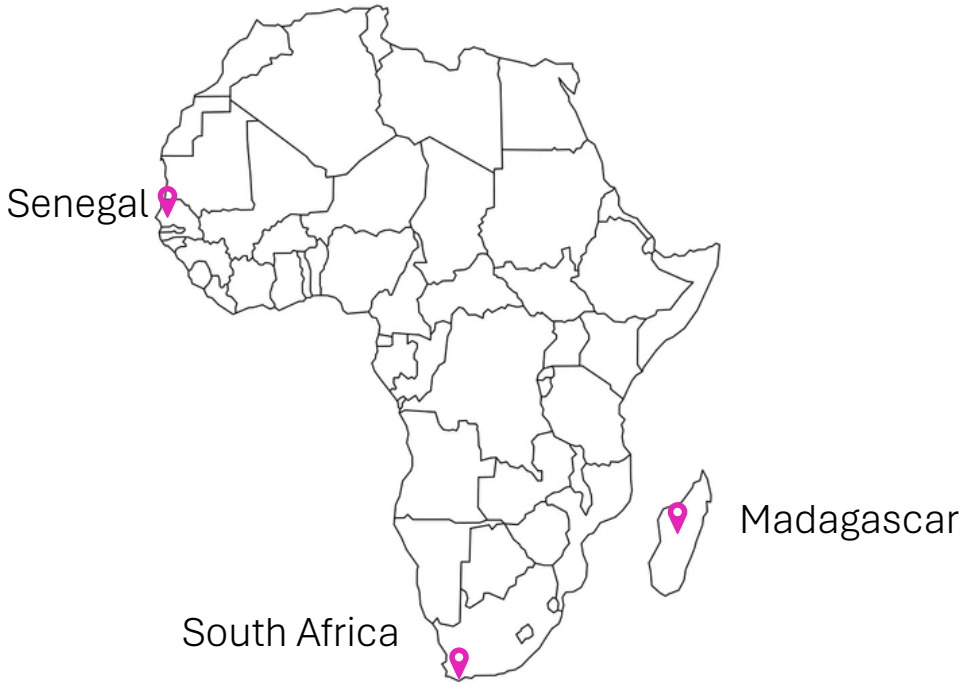
Phase 3 study in neonates in South Africa, Senegal, and Madagascar

MTBVAC in Newborns: Randomized, Double-blind, Controlled Phase 3 Trial to Evaluate the Efficacy, Safety, and Immunogenicity of MTBVAC Administered in Healthy, HIV Unexposed (HU) and HIV Exposed Uninfected (HEU) Newborns in Tuberculosis-endemic Regions of Sub-Saharan Africa [NCT04975178]

Trial duration: 2022-2028

Sample size	N = 7,120 healthy HU and HEU neonates at 6 CRCs (4 in SA, 1 in Mad, 1 Sen)
Control arm	BCG, randomized 1:1 double blind
Follow up duration	24-72 months
Primary objective	To demonstrate efficacy in terms of incidence of MTBVAC against TB disease in healthy HU and HEU newborns compared to BCG
Secondary objective	To assess the safety and reactogenicity of MTBVAC in healthy HU and HEU newborns compared to BCG
Tertiary objective	To assess immunogenicity of MTBVAC in healthy HU and HEU newborns
Exploratory Objective	To identify correlates of protection for MTBVAC To assess the non-specific effects of MTBVAC in healthy HU and HEU newborns compared to BCG: SAEs and MAAEs* due to non-TB infectious diseases and infestations (days 0-42).

*SAE – serious adverse events; MAAE – medically attended adverse event



Status: ongoing

- 6,649 newborns randomized as of 13 April 2026
- 6,529 from South Africa
- Mad and Sen completed recruitment and 1 year follow-up
- 1st interim analysis (IA) set to Q4 2026/Q1 2027

Proposed Phase 3 study among adolescents and adults in India

Randomized, double-blind, placebo-controlled Phase 3 trial to evaluate efficacy, safety, and immunogenicity in Indian adults and adolescents *(design under discussion)*

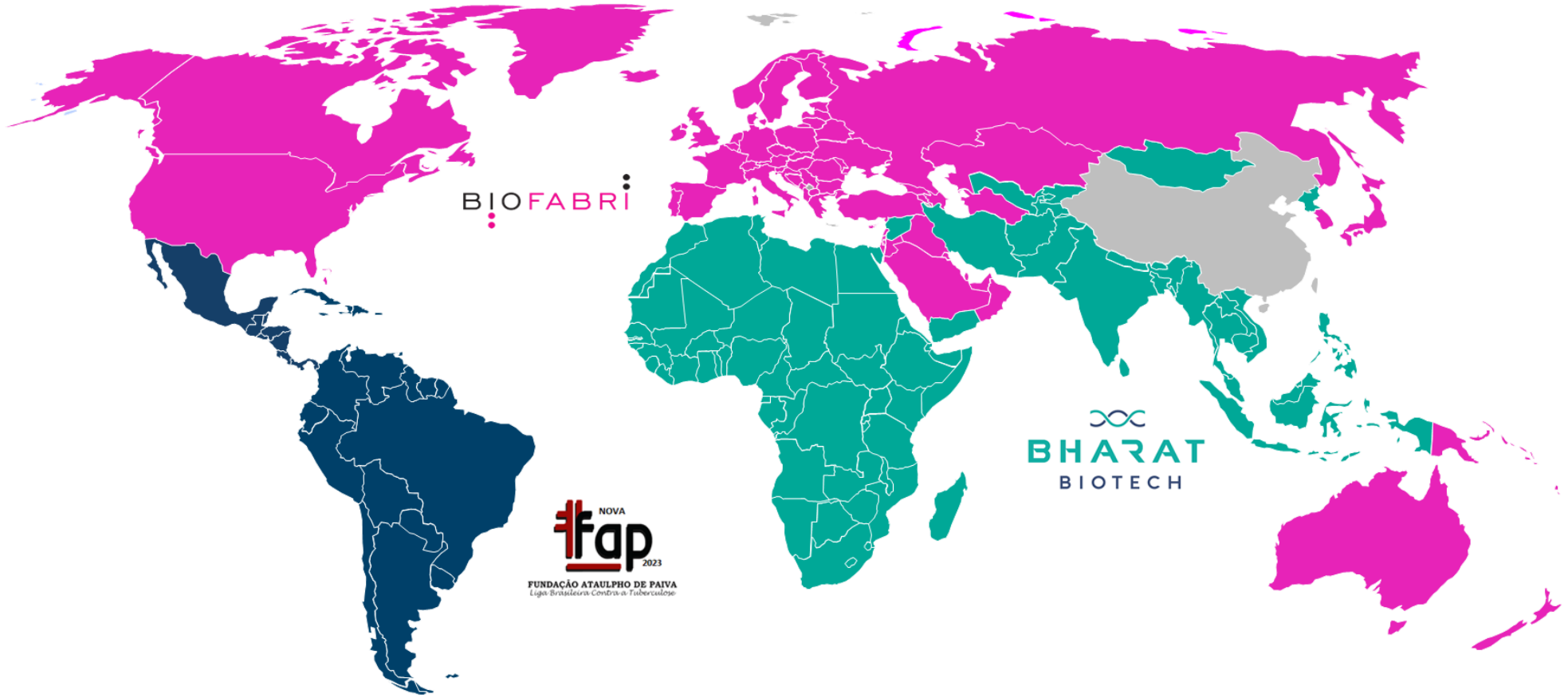
Trial duration: 2026-2031

Sample size	N >25,000 (approx.) adolescent and adult participants QFT+ Safety, Efficacy and Immunogenicity QFT- Safety, Immunogenicity
Control arm	Placebo
Follow up duration	24-48 months
Primary endpoint	PTB diagnosed with one or more signs or symptoms* and at least 2 positive diagnostic tests (culture and/or Xpert MTB/RIF Ultra) from sputum obtained prior to TB treatment
Secondary endpoints	Efficacy (alternative case definitions), safety, immunogenicity

Status: Under development

*unexplained cough, unexplained weight loss, hemoptysis, unexplained fever, night sweats, pleuritic chest pain

MANUFACTURING, SUPPLY AND ACCESS STRATEGY



Biofabri (Spain)	Zone 1	North America, Europe, North Asia, Australia, New Zealand: **85 countries**
FAP (Brazil)	Zone 2	Central & South America: **34 countries**
BBIL (India)	Zone 3	South & Southeast Asia, Africa: **81 countries**
TBD (China)	Zone 4	China, Hong-Kong, Macao, Taiwan

MTBVAC Program: Upcoming in 2026

Clinical Development

- Completing Enrollment of Phase 3 Neonates Trial
- 1st IA on the Phase 3 neonatal trial towards the Q4/2026 - Q1/2027
- Completion of enrolment of Phase 2b adults/adolescents trial towards mid 2026
- Completion of enrolment of Phase 2a PLHIV towards end 2026
- On track for design decisions for Phase 3 in India

Regulatory

- EMA scientific advice planning under the PRIME SCHEME framework
- Planning of national and regional regulatory engagements:
    - South Africa
    - India
    - Brazil and AVAREF planning

Access

- Planning for policy consultations in sub Saharan Africa
- Integration of regulatory and policy considerations into demand estimates with supply planning across regions and manufacturers

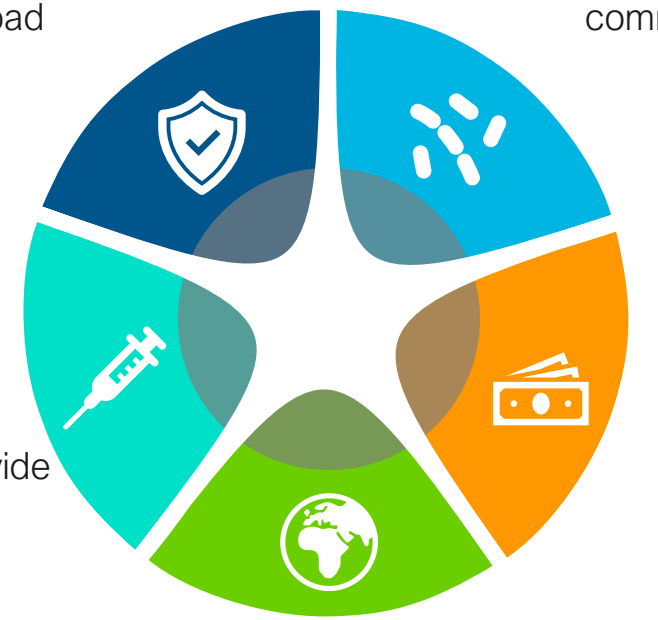
AN ACCESS-INFORMED VALUE PROPOSITION

Broad antigen presentation

Only vaccine directly derived from Mtb isolate in humans, presenting broad range of antigens

Independent sourcing

No supply/price dependence from additional commercial partners



Ease of administration

Single dose schedule to support uptake

One-component vaccine presentation to provide ease of storage and avoid preparation errors

Commitment to affordability

Vaccine platform with relatively cost-effective manufacturing and established commitment to affordable pricing from commercial partners

Global manufacturing footprint

Manufacturing partners lined up in Spain, India, and Brazil; increasing global supply capacity, supply security, and regional equity

In TB Vaccines, TIME IS THE ENEMY

- Two tuberculosis (TB) vaccine candidates are in **Phase 3 clinical trials**, with others in the pipeline
- Manufacturing, distribution, and **global access plans** are underway
- **MTBVAC** shows how partnerships can translate science into access
- **A moment of optimism — but not yet success**

- Phase 3 TB trials are **new territory** for many across the TB ecosystem
- Scientists, clinical sites, labs, CROs, funders, and agencies are **learning in real time**
- The time available to learn is **brief and limited**

- **The core challenge**
- We must know **quickly** if candidates work
- We must know **even faster** if they do not — to move to the next option
- **Time is our enemy…**

Accelerate Now — Or Lose Ground

1. **Accelerate Phase 3 trials**
   - Reach **deeper consensus on diagnosis**
   - Harmonize endpoints — **not many, just the right ones**
   - Avoid unnecessary complexity that delays execution
2. **Strengthen execution**
   - Increase operational speed and coordination
   - Reinforce laboratory systems and personnel training
3. **Enable faster decisions**
   - Create frameworks for **faster regulatory filings and reviews**
   - Streamline processes at leading agencies and beyond

Why this matters

- Every week and month of delay pushes us **further from decisive data**
- Meanwhile, **people are infected and patients die**

TIME IS THE ONLY ENEMY

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TBVI

iavi

Coefficient Giving

Fred Hutch Cancer Center

BHARAT BIOTECH

NOVA ftap 2023 FUNDAÇÃO ATAULPHO DE PAIVA Liga Brasileira Contra a Tuberculose

Gates Foundation

Trial Participants

Clinical Trial Sites and Lab personnel

TARGET PRODUCT PROFILE: neonates

Attribute	Upside Target	Minimally Acceptable Target
Indication for use	Prevention of TB disease	
Target population	All newborns	HIV-non-infected newborns
Relative efficacy (compared to BCG)	75%	50%
Duration of protection	≥10 years	≥ 5 years
Route of administration	Intradermal (ID)	
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TARGET PRODUCT PROFILE: adolescents and adults

Attribute	Upside Target	Minimally Acceptable Target
Indication for use	Prevention of active pulmonary TB disease	
Target population	Adolescents and adults	
Efficacy (compared to placebo)	VE≥ 50%	
Duration of protection	≥ 10 years	≥ 2 years
Route of administration	Intradermal (ID)	
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