7TH GLOBAL FORUM ON TB VACCINES | 8-10 October 2024 Rio de Janeiro, Brazil

Driving innovation from discovery to access

MTBVAC - Late Stage Clinical Development

Advancing TB Vaccine Clinical Development: Learning from Experience & Looking to the Future

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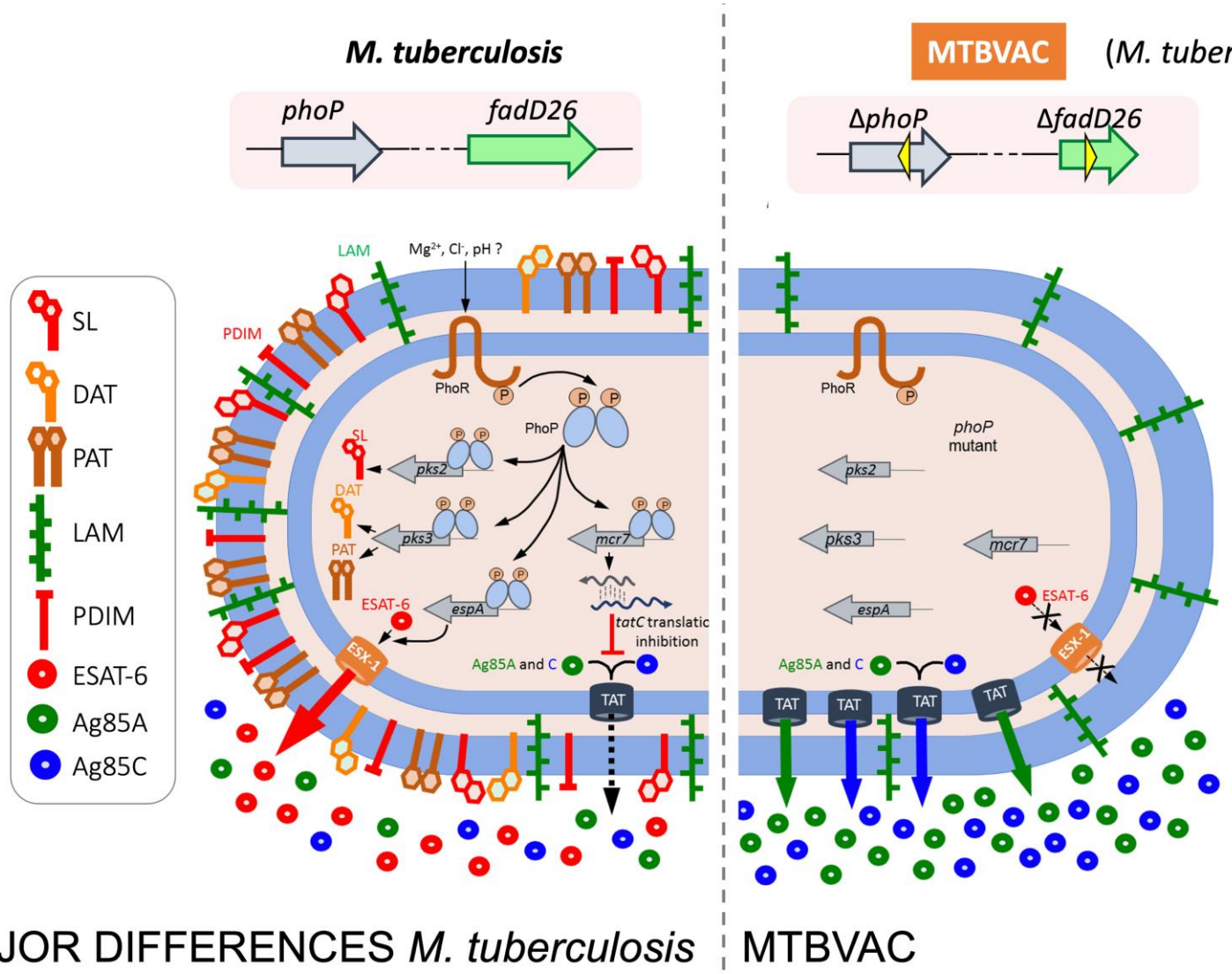
MTBVAC Live Vaccine - Two Stable Deletions in Independent MTB Major Virulence Factors Without Antibiotic Resistance Markers



phoP: controls expression 2% of MTB genes

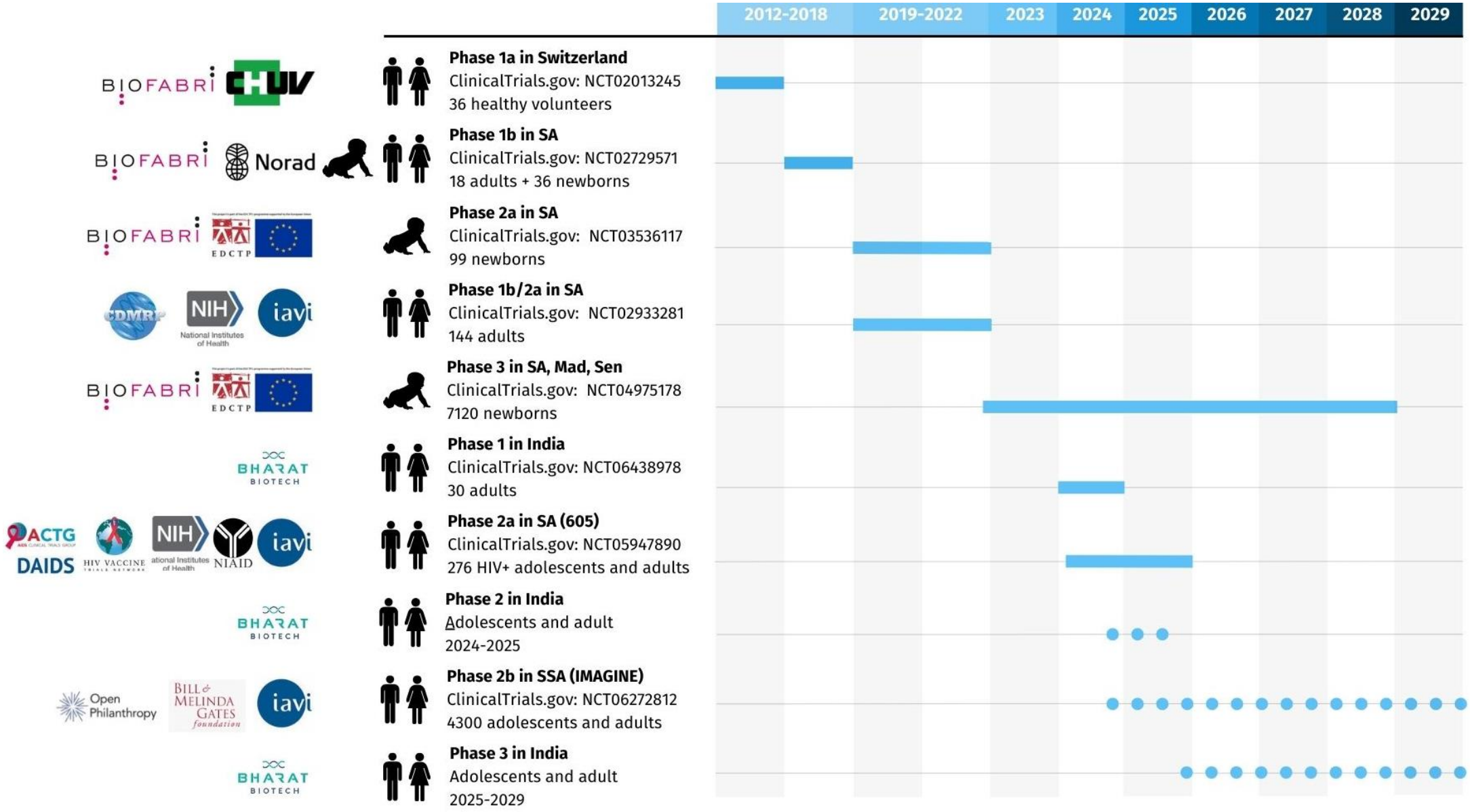
fadD26: synthesis PDIM Major Virulence Lipid in MTB

Major difference MTBVAC/ BCG contains RD1:

ESAT6/CFP10/PPE68: 311 epitopes

J Gonzalo Asensio

MTBVAC Timeline



MTBVAC *The Lancet Respiratory Diseases Publications*

Phase 1a in adults in Switzerland

Safety of human immunisation with a live-attenuated Mycobacterium tuberculosis vaccine: a randomised, double-blind, controlled phase I trial

François Spertini [1], Régine Audran [2], Reza Chakour [2], Olfa Karoui [2], Viviane Steiner-Monard [2], Anne-Christine Thierry [2], Carole E Mayor [2], Nils Rettby [3], Katia Jaton [4], Laure Vallotton [5], Catherine Lazor-Blanchet [6], Juana Doce [7], Eugenia Puentes [7], Dessislava Marinova [8], Nacho Aguilo [8], Carlos Martin [9]

Affiliations + expand

PMID: 26598141 DOI: 10.1016/S2213-2600(15)00435-X

Published 2015

Dr. F. Spertini

Main conclusion:

MTBVAC is as safe and immunogenic as BCG in healthy adults, not BCG vaccinated and HIV negative.

Phase 1b in adults and newborns in South Africa

Live-attenuated Mycobacterium tuberculosis vaccine MTBVAC versus BCG in adults and neonates: a randomised controlled, double-blind dose-escalation trial

Michele Tameris [1], Helen Mearns [1], Adam Penn-Nicholson [1], Yolande Gregg [1], Nicole Bilek [1], Simbarashe Mabwe [1], Hennie Geldenhuys [1], Justin Shenje [1], Angelique Kany Kany Luabeya [1], Ingrid Murillo [2], Juana Doce [2], Nacho Aguilo [3], Dessislava Marinova [3], Eugenia Puentes [2], Esteban Rodríguez [2], Jesús Gonzalo-Asensio [3], Bernard Fritzell [4], Jelle Thole [4], Carlos Martin [5], Thomas J Scriba [1], Mark Hatherill [6]; MTBVAC Clinical Trial Team

Collaborators, Affiliations + expand

PMID: 31416768 DOI: 10.1016/S2213-2600(19)30251-6

Published 2019

Dr. M Tameris

Main conclusion:

MTBVAC is as safe as BCG and more immunogenic than BCG in neonates.

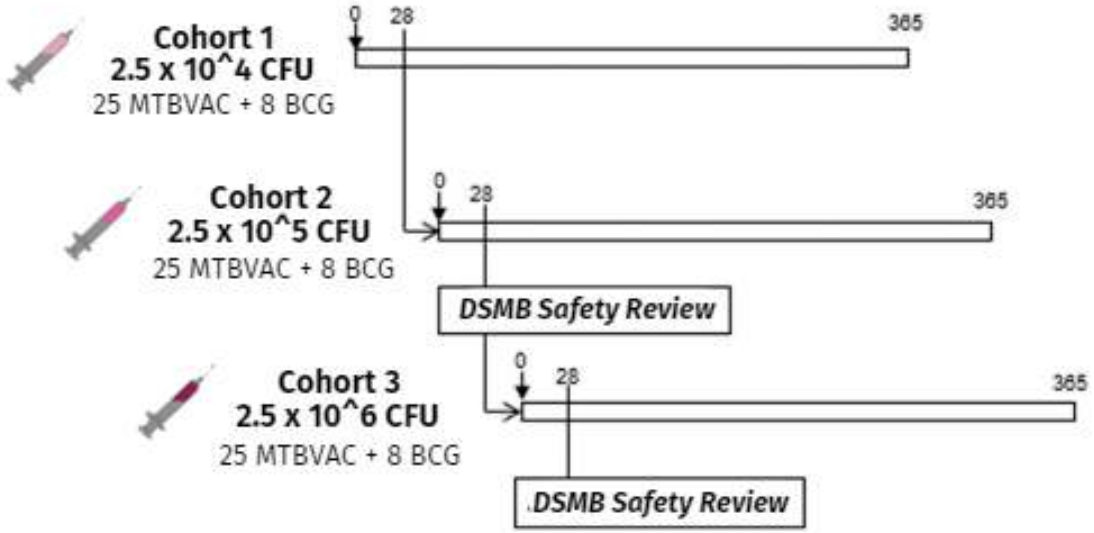
MTBVAC in newborns **- Phase 2a** RIA2016V-1637

Completed, submitted for publication

A Phase 2a Randomized Controlled **Dose-Defining** Trial of the **Safety** and **Immunogenicity** of MTBVAC in Healthy, BCG Naïve, HIV Unexposed, South African Newborns.

Key points:

- Sample size - **99** ppts **in 1 site**
- **Single dose, intradermal** (**ID**)



MTBVAC in newborns **- Phase 2a** RIA2016V-1637

Completed, submitted for publication

Main conclusions:

- All three doses seemed safe and well tolerated (10^4, 10^5 and 10^6)
- MTBVAC is as safe as BCG and more immunogenic than BCG in newborns

Dose selected for the Phase 3 → **2.5 x 10^5 CFU**

MTBVAC in newborns **- Phase 2a** RIA2016V-1637

Completed, submitted for publication

Main conclusions:

- All three doses seemed safe and well tolerated (10^4, 10^5 and 10^6)
- MTBVAC is as safe as BCG and more immunogenic than BCG in newborns

Dose selected for the Phase 3 → **2.5 x 10^5 CFU**

In concordance with WHO recommendations, the 2.5x10^5 CFU MTBVAC dose was selected for phase 3 efficacy evaluation compared to BCG vaccination in infants.

Please refer to Poster Session room for further information on this study.

MTBVAC A-050 in adults **- Phase 1b/2a**

Completed, submitted for publication

Live-attenuated *M. tuberculosis* vaccine, MTBVAC, in adults with or without *M. tuberculosis* sensitization: a Phase 1b/2a randomized, controlled, double-blind, **dose-escalation trial**

Key points:

- Sample size - **144** ppts **in 1 site**
- Single dose, intradermal **(ID)**
- **8** Cohorts - QFT + and QFT - with 4 doses each to evaluate dose level:

MTBVAC A-050 in adults **- Phase 1b/2a**

Completed, submitted for publication

Main conclusions:

- There were no serious side effects linked to the MTBVAC vaccine.
- Dose 5 x 10^5 CFU is as safe as BCG and more immunogenic than BCG in QFT negative and what is more important, in QFT positive cohorts.

Dose selected for future studies → **5 x 10^5 CFU**

MTBVAC A-050 in adults **- Phase 1b/2a**

Completed, submitted for publication

Main conclusions:

- There were no serious side effects linked to the MTBVAC vaccine.
- Dose 5 x 10^5 CFU is as safe as BCG and more immunogenic than BCG in QFT negative and what is more important, in QFT positive cohorts.

Dose selected for future studies → **5 x 10^5 CFU**

The results show that the efficacy of MTBVAC can be studied in both QFT positive and negative efficacy trials.

Please refer to Poster Session room for further information on this study.

MTBVACN3 in neonates **– Phase 3** RIA2019S-2652

Ongoing

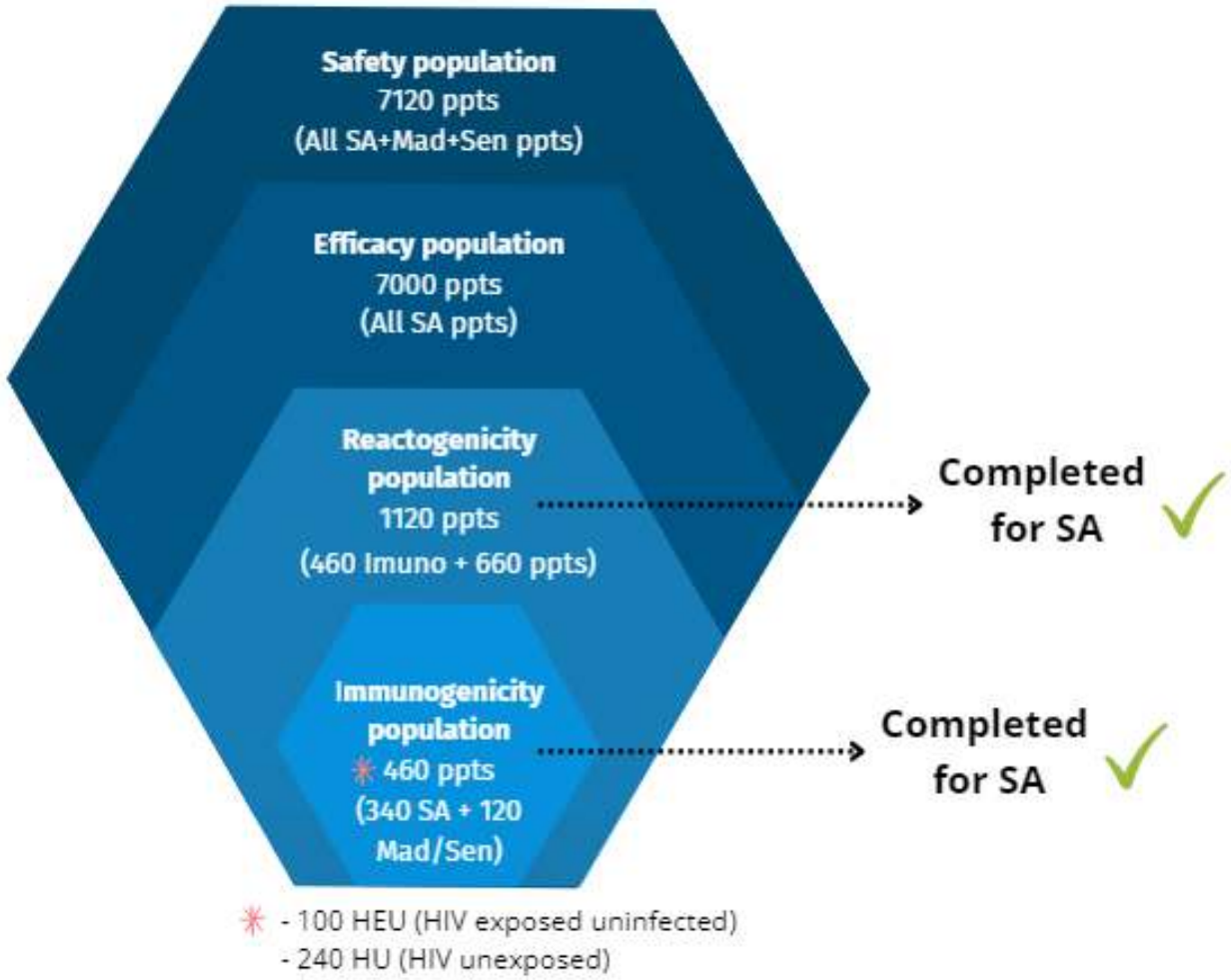
Randomized, **Double blind**, Controlled Phase 3 to evaluate the **Efficacy**, **Safety** and **Immunogenicity** of MTBVAC administered in healthy HIV unexposed uninfected and HIV exposed uninfected newborns in Tuberculosis-Endemic Regions of Sub-Saharan Africa.

MTBVACN3 in neonates **- Phase** RIA2019S-2652

Ongoing

This project is part of the EDCTP2 programme supported by the European Union
EDCTP
BIOFABRI RIA2019S-2652 MTBVACN3

Study Population



Study Sites

3000 vaccinated babies

42.1% of total target

by 19 September 2024

MTBVACN3 in neonates **- Phase** RIA2019S-2652

Ongoing

This project is part of the EDCTP2 programme supported by the European Union
EDCTP
BIOFABRI RIA2019S-2652 MTBVACN3

Key points:

- Sample size - **7120** ppts in **6 sites**
- Single dose, intradermal (**ID**)
- Control - BCG vaccine
- Follow up - 2- 6 years

- **DSMB** (Data Safety Monitoring Board) - Periodically reviews cumulative safety data
  - 3 meetings held by protocol - “No safety concerns raised, and study should continue as planned.”

- **AC** (Adjudication Committee) - Validates TB cases reported by sites.

Milestones:

- **1st** interim analyses - 49 adjudicated TB cases
- **2nd** interim analyses - 97 adjudicated TB cases

HVTN 605 in HIV+ Adolescents and adults **- Phase 2a** in SA

Ongoing

A phase 2a clinical trial to evaluate the **safety** and **immunogenicity** of MTBVAC in adolescents and adults living with and without HIV in South Africa.

Study Sites

Key points:

- Sample size - **276 ppts** (12 - 55 y) in **16 sites**
- Single dose, intradermal (**ID**)
- Control - BCG vaccine
- Follow up - 1 year
- Cohorts:
  - 1st HIV –
  - 2nd HIV + , CD4 T-cell count ≥ 200 cells/mm3

Safety data assessment

  - 3rd HIV +, CD4 T-cell count ≥ 100 cells/mm3

If the results of this study show that it is safe in HIV + group, it will be allowed to use MTBVAC in this population.

Phase 2b in SSA : **IMAGINE** in Adolescents and Adults

Investigation of **M**TBVAC toward **A**ccelerating **G**lobal **I**mmunization for a **N**eglected **E**pidemic

A Phase 2b, double-blind, randomized, placebo-controlled study to evaluate the **efficacy, safety** and **immunogenicity** of a candidate tuberculosis (TB) vaccine, MTBVAC, against TB disease in **interferon gamma release assay positive** adolescents and adults aged 14-45 years, living in a TB endemic region.

Key points:

- Sample size - **4300 ppts** (14 - 45 y) in **15 sites**
- BCG vaccinated in infancy
- Single dose, intradermal (**ID**)
- Control – Placebo
- Follow up - 2 years
- Protocol amendment Approval – 1st Oct 2024

Please refer to Poster Session room for further information on this study.

BBIL/BBV169-I/2023 in Adults **- Phase 1** in India

Completed

Phase I Clinical Trial, open label to Assess the **Safety, Reactogenicity, Tolerability** and **Immunogenicity** of a Tuberculosis Vaccine BBV169 (MTBVAC), in Healthy Indian Adults.

Key points:

- Sample size - **30** ppts (18 - 65 y) - **Recruitment has ended**
- 1 site
- Single dose, intradermal (**ID**)
- Cohort - Healthy, BCG vaccinated, HIV negative
- Follow up - 6M
- Pending preliminary results

BBIL/MTBVAC-II/2024 in Adults **- Phase 2** in India

A Phase II, Randomized, Double-blind Trial to Assess the **Safety** and **Immunogenicity** of MTBVAC (BBV169), with BCG vaccine as a comparator in Healthy adolescent and adult populations.

Key points:

- Sample size - **164 ppts** (12-65 y)
- Single dose, intradermal (**ID**)
- Cohort - QFT + and QFT –
- Control - BCG vaccine
- Follow up - 6M
- 1st milestone: Interim analysis at D28 visit - DSMB safety analysis
- Enrollment to start in Q4 2024

Study Sites

BBIL/MTBVAC-II/2024 in Adults **- Phase 2** in India

A Phase II, Randomized, Double-blind Trial to Assess the **Safety** and **Immunogenicity** of MTBVAC (BBV169), with BCG vaccine as a comparator in Healthy adolescent and adult populations.

Key points:

- Sample size - **164 ppts** (12-65 y)
- Single dose, intradermal (**ID**)
- Cohort - QFT + and QFT –
- Control - BCG vaccine
- Follow up - 6M
- 1st milestone: Interim analysis at D28 visit - DSMB safety analysis
- Enrollment to start in Q4 2024

Phase 3 planned to start in Q3/Q4 2025.

Study Sites

Capacity Building & Tech. Transfer

Madagascar and Senegal

CTs in LMICs:

- Creation of MTBVAC consortium
- Initiation of TB vaccine trials preparedness in Madagascar and Senegal

Capacity building

- ✓ Quality assurance, equipment maintenance
- ✓ Staff training and education
- ✓ Logistical and infrastructures
- ✓ Management of essential documents and source document (SOP, Log, Form, Document)
- ✓ Improving ethics and pharmacovigilance skills

IPM and **CRB-EPLS** executed **capacity building** methods and technology transfer validation steps during Phase2a to ensure proficiency and **activation for Phase3 in neonates**.

Please refer to Poster Session room for further information on this study.

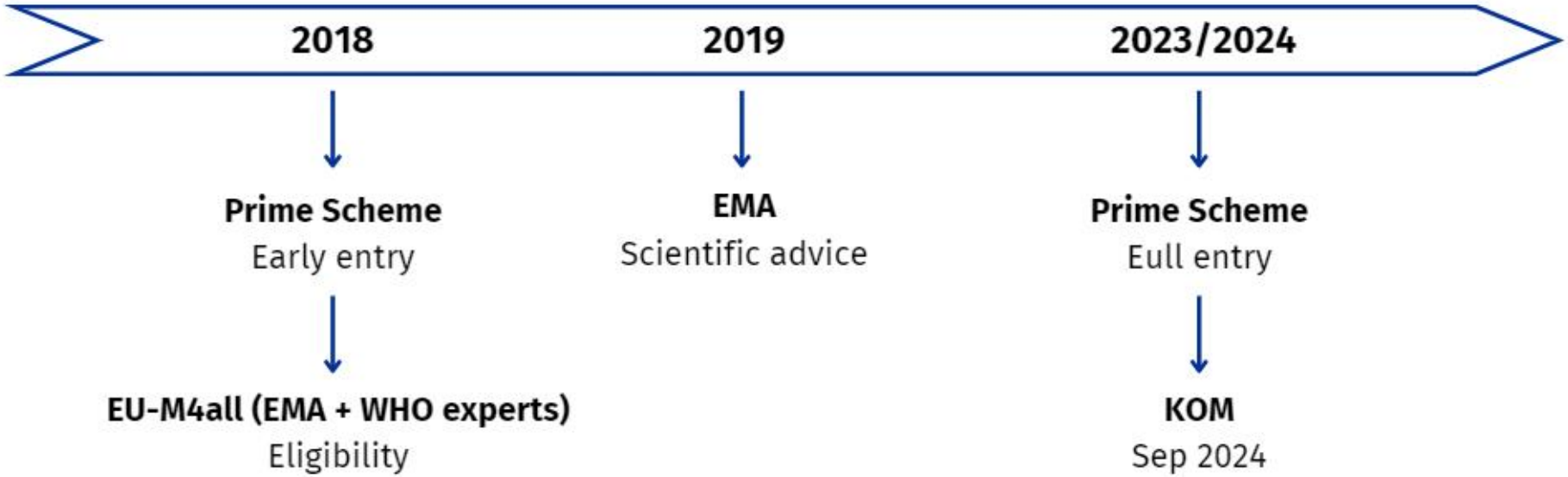
PRIME SCHEME by EMA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

BIOFABRI

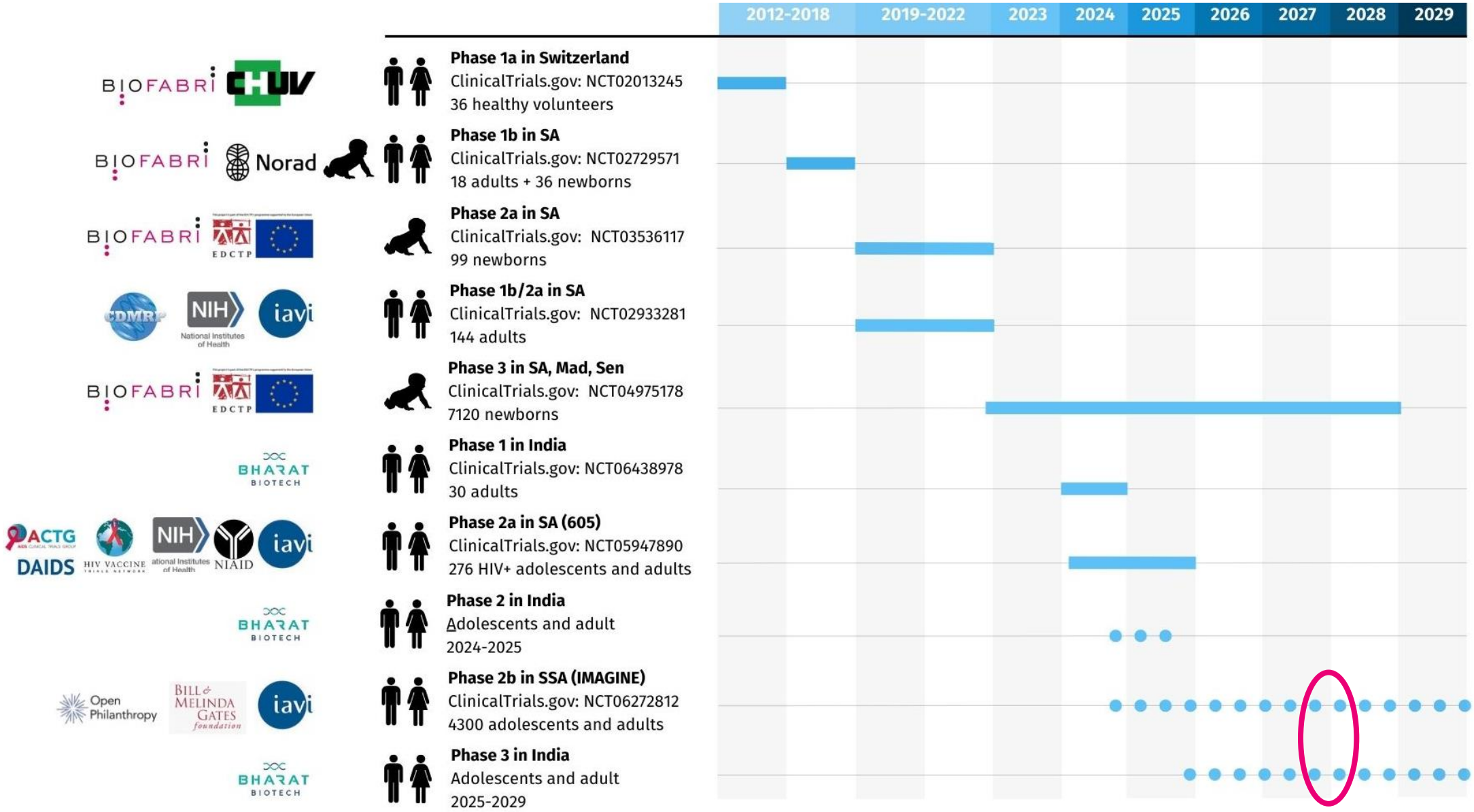
PRIME: Priority Medicines

PRIME is a scheme run by the European Medicines Agency (EMA) to enhance support for the development of medicines that target an unmet medical need. This voluntary scheme is based on enhanced interaction and early dialogue with developers of promising medicines; to optimize development plans and speed up evaluation so these medicines can reach patients earlier.



MTBVAC Timeline

¡¡¡ BIG THANKS !!!!



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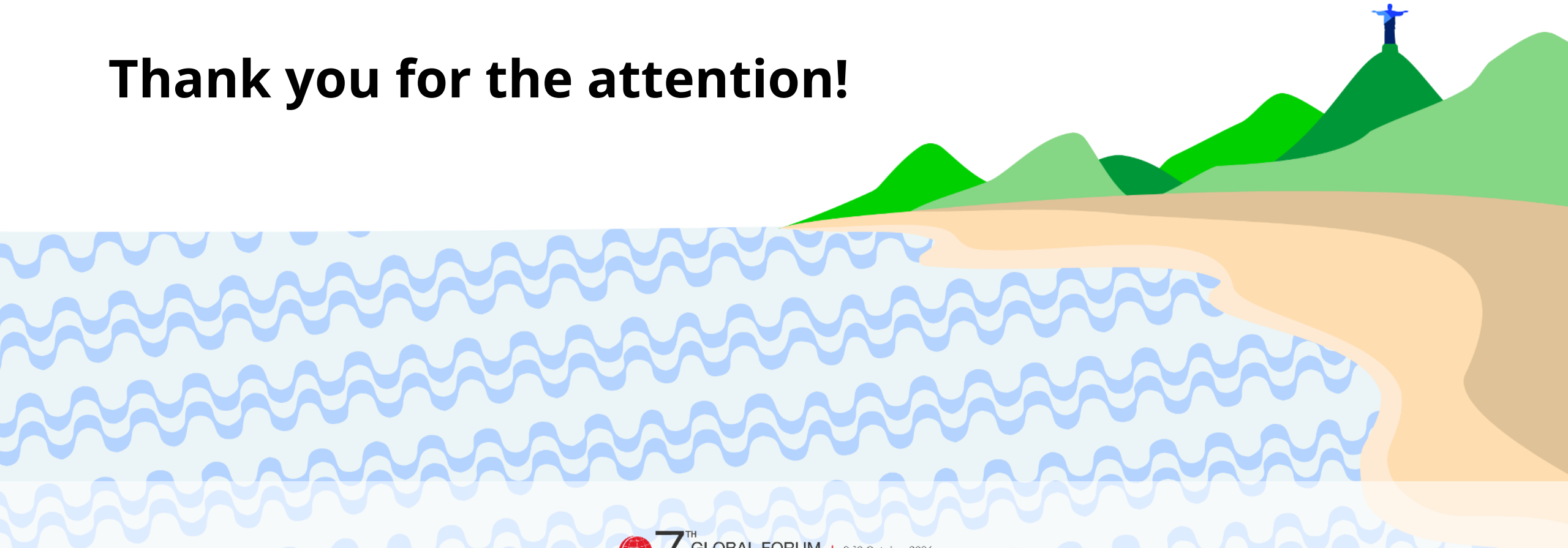

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Driving innovation from discovery to access

An international convening of the

Stop TB Partnership WORKING GROUP ON NEW TB VACCINES

iavi Translating science into global health impact

TBVI TuBerculosis Vaccine Initiative

Organized in collaboration with

SUS MINISTÉRIO DA SAÚDE GOVERNO FEDERAL BRASIL UNIÃO E RECONSTRUÇÃO

REDE-TB