TB VACCINE R&D: STATE OF THE FIELD

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Stop TB Working Group on New Vaccines Annual Meeting
Paris, France
November 14, 2023
WHY ARE BETTER TB VACCINES URGENTLY NEEDED?
In 2022: 10.6 million new cases of TB and 1.3 million deaths

- 8-9% of TB cases and ~13% of TB deaths are in persons living with HIV

TB incidence **increased** by ~3.9% from 2020-2022

- follows ~2% per year **declines** from 2010-2020

BCG helps protect young children from severe forms of TB

- but does not reliably protect adolescents and adults and is not controlling the epidemic


*Effective vaccines are a critical unmet public health need*
ADOLESCENTS AND YOUNG ADULTS ARE THE HIGHEST PRIORITY TARGET FOR TB VACCINES because they are the main source of M.tb transmission.

Global estimates of TB incidence (black outline) and case notifications of people newly diagnosed with TB disaggregated by age and sex (female in purple; male in orange), 2022

THE GLOBAL CLINICAL PORTFOLIO OF TB VACCINE CANDIDATES
17 CANDIDATES IN CLINICAL DEVELOPMENT

TB Vaccine Pipeline

Vaccine candidates under clinical development

There are 16 vaccine candidates in the pipeline as of September 2023, of which 11 are in active trials. The candidates are placed under the phase which corresponds to the most advanced ongoing or completed trial.

- **Platform**
  - Mycobacterial - Live attenuated
  - Mycobacterial - Inactivated
  - Viral vector
  - Protein/Adjuvant
  - RNA

- **Candidate target population**
  - Elderly
  - Adults
  - Adolescents
  - Children
  - Infants
  - People living with HIV
  - -mTB People without mTB infection
  - +mTB People with mTB infection
  - aTBd People with active TB disease
  - MDR People with MDR-TB
  - cTB People cured of active TB

- **Primary candidate indication**
  - POI Prevention of Infection
  - POD Prevention of Disease
  - POR Prevention of Recurrence
  - Thp Therapeutic

- **Trial status**
  - ✓ Active trials
  - ✗ No active trials

For the full list of completed trials for each candidate, visit [www.newtbvaccines.org/tb-vaccine-pipeline](http://www.newtbvaccines.org/tb-vaccine-pipeline/)

Last update: 28 September 2023
Modified by AMG November 2023

*BCG appears twice in the pipeline to distinguish between the investigation of its use in BCG-naïve individuals (traveler vaccination) and in individuals who have previously been vaccinated with BCG (revaccination).*
TB Vaccine Pipeline

Active clinical trials of TB vaccine candidates

There are 11 active clinical trials across nine candidates as of October 2022.

Platform
- Mycobacterial - Live attenuated
- Mycobacterial - Inactivated
- Viral vector
- Protein/Adjuvant

mRNA

Trial target population
- Elderly
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Primary trial indication
- Sf Safety
- POD Prevention of Infection
- POI Prevention of Disease
- POR Prevention of Recurrence
- Thp Therapeutic

Trials in planning:
- H107/CAF10b Ph1a/b
- MTBVAC Ph2b (adolescents/adults)
- M72/AS01E Ph 3

Information reported by vaccine sponsors or found in clinical trial registries or other public sources. For the full list of completed trials for each candidate, visit www.nexttbvaccines.org/tb-vaccine-pipeline/
## Table: Anticipated Bolus of Efficacy Results 2024-2028

<table>
<thead>
<tr>
<th>Vx candidate</th>
<th>Trial endpoint</th>
<th>Trial phase</th>
<th>Trial population</th>
<th>Results due</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>VPM1002 also, IMMUVAC (MIP)</td>
<td>POD</td>
<td>Ph3</td>
<td>HHC (~13,000)</td>
<td>2024</td>
<td></td>
</tr>
<tr>
<td></td>
<td>POR</td>
<td>Ph2/3</td>
<td>Adults on rx (~2000)</td>
<td>2024</td>
<td></td>
</tr>
<tr>
<td></td>
<td>POI</td>
<td>Ph3</td>
<td>Infants (~6900)</td>
<td>2026</td>
<td>Non-inferiority to BCG</td>
</tr>
<tr>
<td>MTBVAC</td>
<td>POD (infants)</td>
<td>Ph3</td>
<td>Infants (~7100)</td>
<td>4Q 2028</td>
<td>Superiority to BCG</td>
</tr>
<tr>
<td></td>
<td>POD (adol/adult)</td>
<td>Ph2b</td>
<td>Adol/adult (14-45; ~4300)</td>
<td>IA: 2027?</td>
<td>In planning – starting mid-2024-T</td>
</tr>
<tr>
<td>BCG revac</td>
<td>POI</td>
<td>Ph3</td>
<td>Adol/adult (15-44; ~26,000)</td>
<td>IA: 2027-8?</td>
<td>Primary – 2024; final - 2026</td>
</tr>
<tr>
<td>M72/AS01_E</td>
<td>POD</td>
<td>Ph3</td>
<td>Cured adults</td>
<td>2023-4</td>
<td></td>
</tr>
<tr>
<td>ID93+GLA-SE / QPT101</td>
<td>POD</td>
<td>Ph2b/3</td>
<td>Adol/adult in S. Korea</td>
<td>?</td>
<td>In planning - Starting 4Q2023-T</td>
</tr>
<tr>
<td>RUTI</td>
<td>POR</td>
<td>Ph2b</td>
<td>Adults on rx</td>
<td>2025</td>
<td></td>
</tr>
<tr>
<td>RUTI</td>
<td>Adjunct to rx (improved outcomes)</td>
<td>Ph2b</td>
<td>Adults on rx</td>
<td>2025</td>
<td></td>
</tr>
<tr>
<td>GAMTBVAC</td>
<td>POD</td>
<td>Ph3</td>
<td>HIV-, Mtb- adults 18-45 (~7100); TB incid.&gt;30/100,000)</td>
<td>4Q 2025</td>
<td></td>
</tr>
</tbody>
</table>
A ROBUST DEVELOPMENT PIPELINE

PRECLINICAL

PHASE 1

PHASE 2

PHASE 3
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Last update: 02 February 2023
Modified by AMG November 2023
GAPS AND CHALLENGES
MAJOR CHALLENGES AND GAPS IN TB VACCINE R&D

- Complex pathogen expressing ~4000 antigens; protective epitopes/antigens largely unknown
- To date, no identified vaccine-induced Correlate(s) of Protection in humans
- Human protective immune responses only partially understood
- No reproducibly predictive animal model(s) human challenge model established
- Pipeline of candidates not adequately robust – inverted pipeline
- Effects of HIV status, infection (IGRA/TST) status, age and geography on vaccine efficacy must be determined for each vaccine
- Inadequate capacity for multiple, overlapping registration-quality efficacy trials
- Preparation for access, adoption and delivery to end users just beginning
- Inadequate funding and political will
BUILDING A MORE ROBUST “NEXT GENERATION” PIPELINE

- Novel Platforms: mRNA, nanoemulsions, viral vectors
- New Formulations
- Routes of administration: mucosal (intranasal, aerosol)
- Novel Adjuvants
- Human protective antigen identification
- Discover Correlates of Protection
- Optimizing animal models
- Human Challenge Model
END-TO-END DEVELOPMENT OF TB VACCINES

Groundwork being laid:

Selected examples:
- Preferred Product Characteristics
- R&D Roadmap to Phase 3 (AIGHD, EDCTP)
- Roadmap from Licensure to Implementation (WHO)
- Investment Case for a New TB Vaccine (full value assessment) (WHO)
- Evidence Considerations for Vaccine Policy (WHO)
- TB Vaccine Market Analysis (Wellcome Trust)
- National TB Vaccine Policy Project (BMGF)
- TB Vx Implementation Planning Landscape and Gap Analysis (*underway with WHO*)
THANK YOU!
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