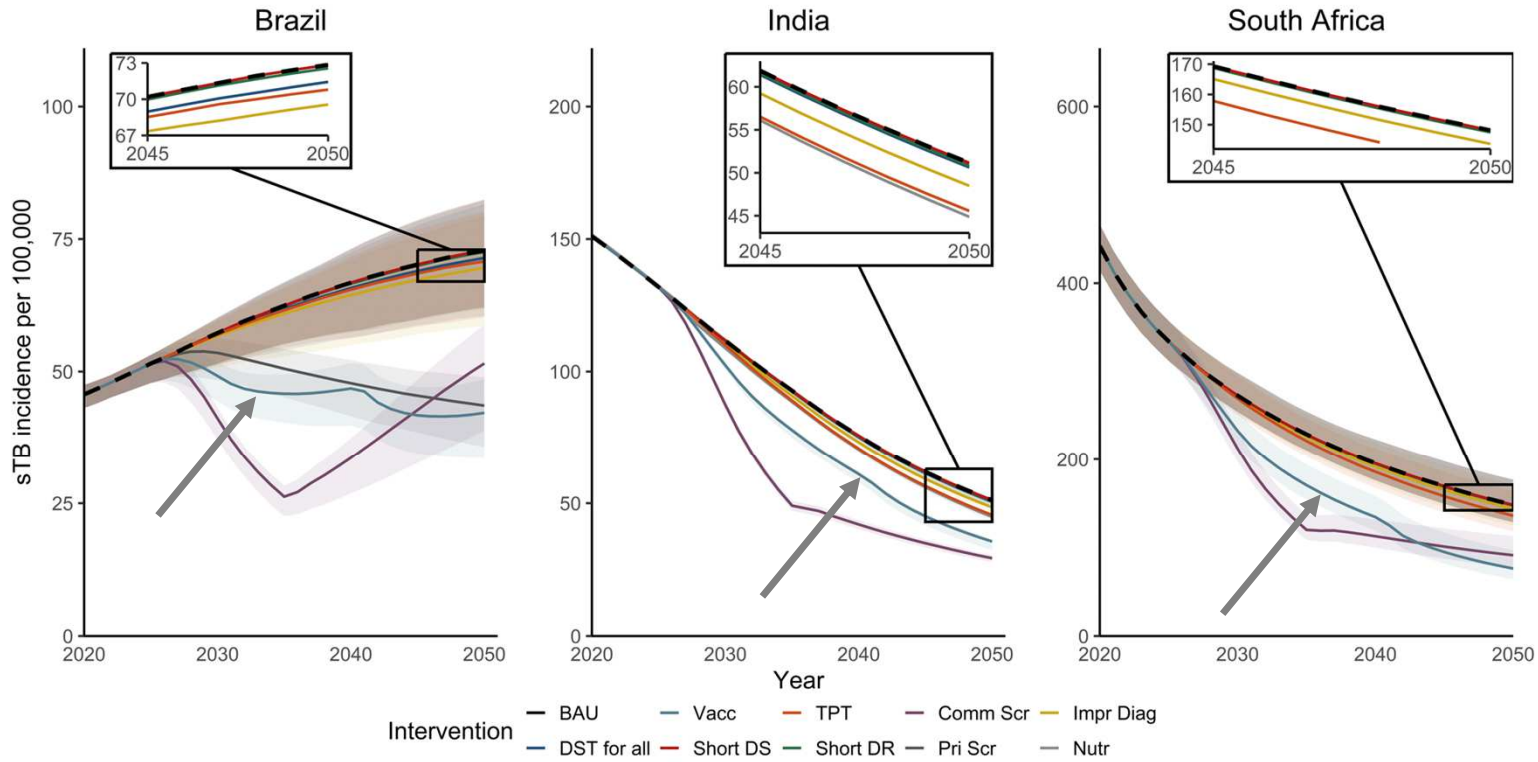
TB vaccines: where are we now?

Willem Hanekom

Executive director, Africa Health Research Institute

A new vaccine for adolescents and adults would be the most impactful intervention to control TB.



BAU = Business-As-Usual, Vacc = Vaccination, TPT = Tuberculosis Preventive Treatment, Comm Scr = Community-wide screening, Impr Diag = Improved diagnosis in clinics, DST for all = Drug Susceptibility Testing for all clinic-diagnosed individuals, Short DS = Shortened treatment for Drug Susceptible TB,

Horton, et al. medRxiv 2026.

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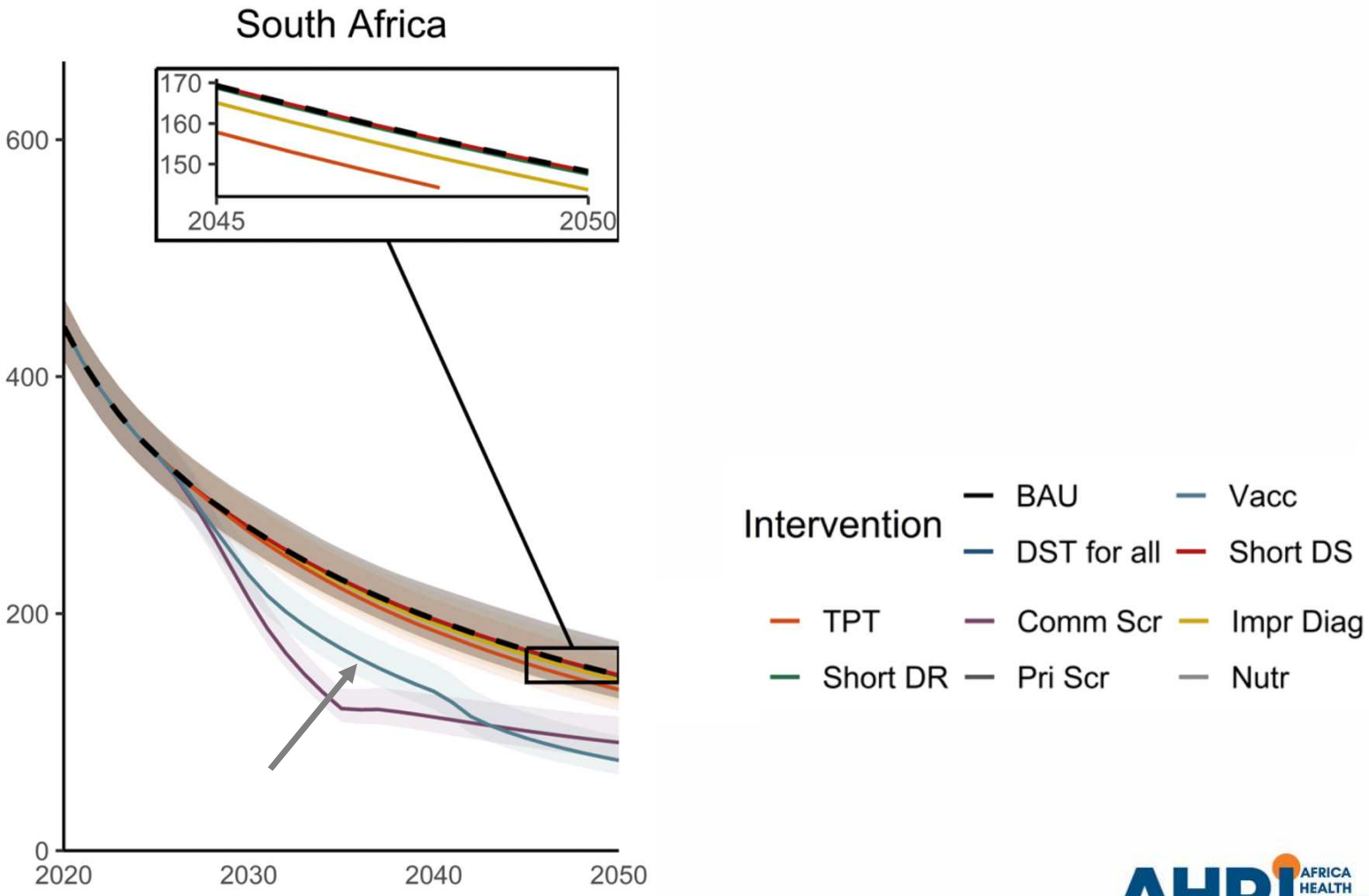
A new vaccine that targets adolescents and adults.



Horton, et al. medRxiv 2026.

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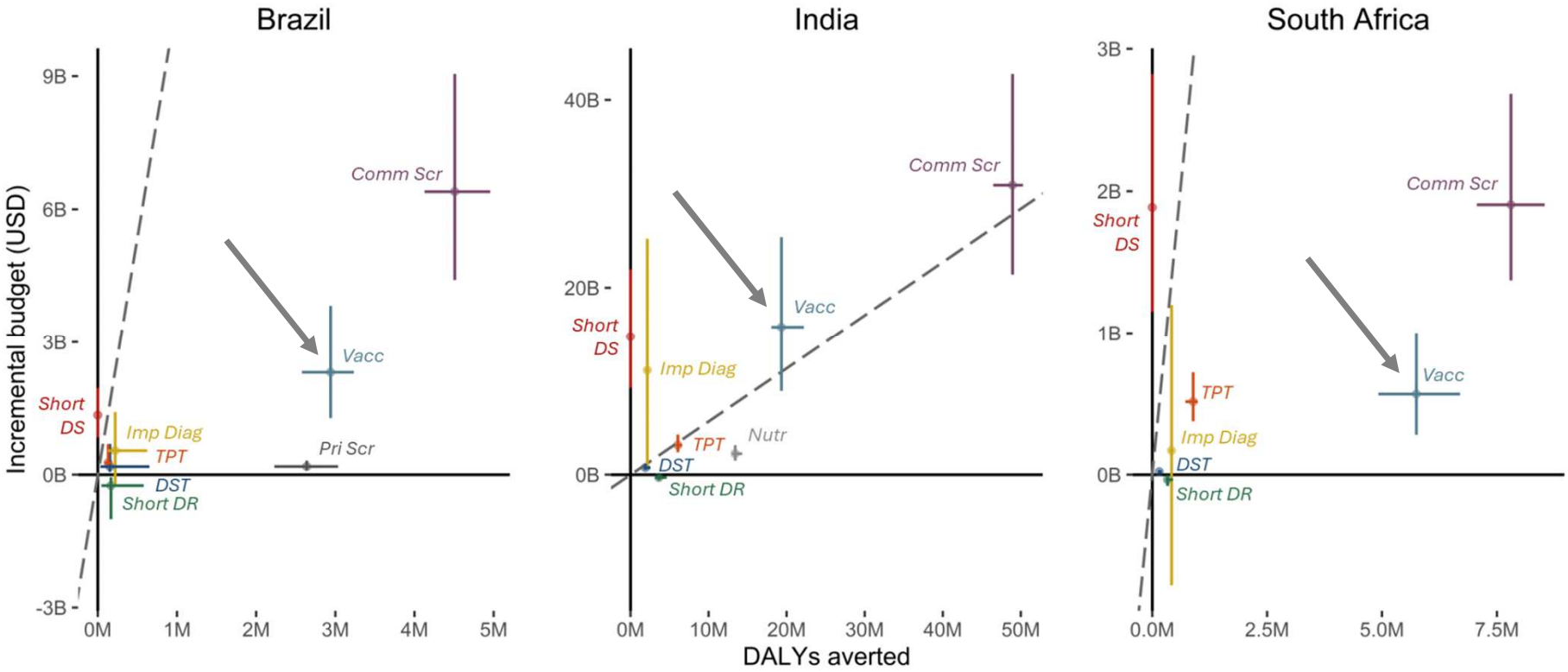
A new vaccine that targets adolescents and adults will be cost-effective.



Horton, et al. medRxiv 2026.

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80%
60%
BCG

WHO Preferred Product Characteristics for New Tuberculosis Vaccines

DEPARTMENT OF IMMUNIZATION, VACCINES AND BIOLOGICALS

Family, Womens's and Children's Health (FWC)

World Health Organization

Infants and children

Adolescents and adults

Even 20% efficacy against adolescent and adult disease would have an impact.

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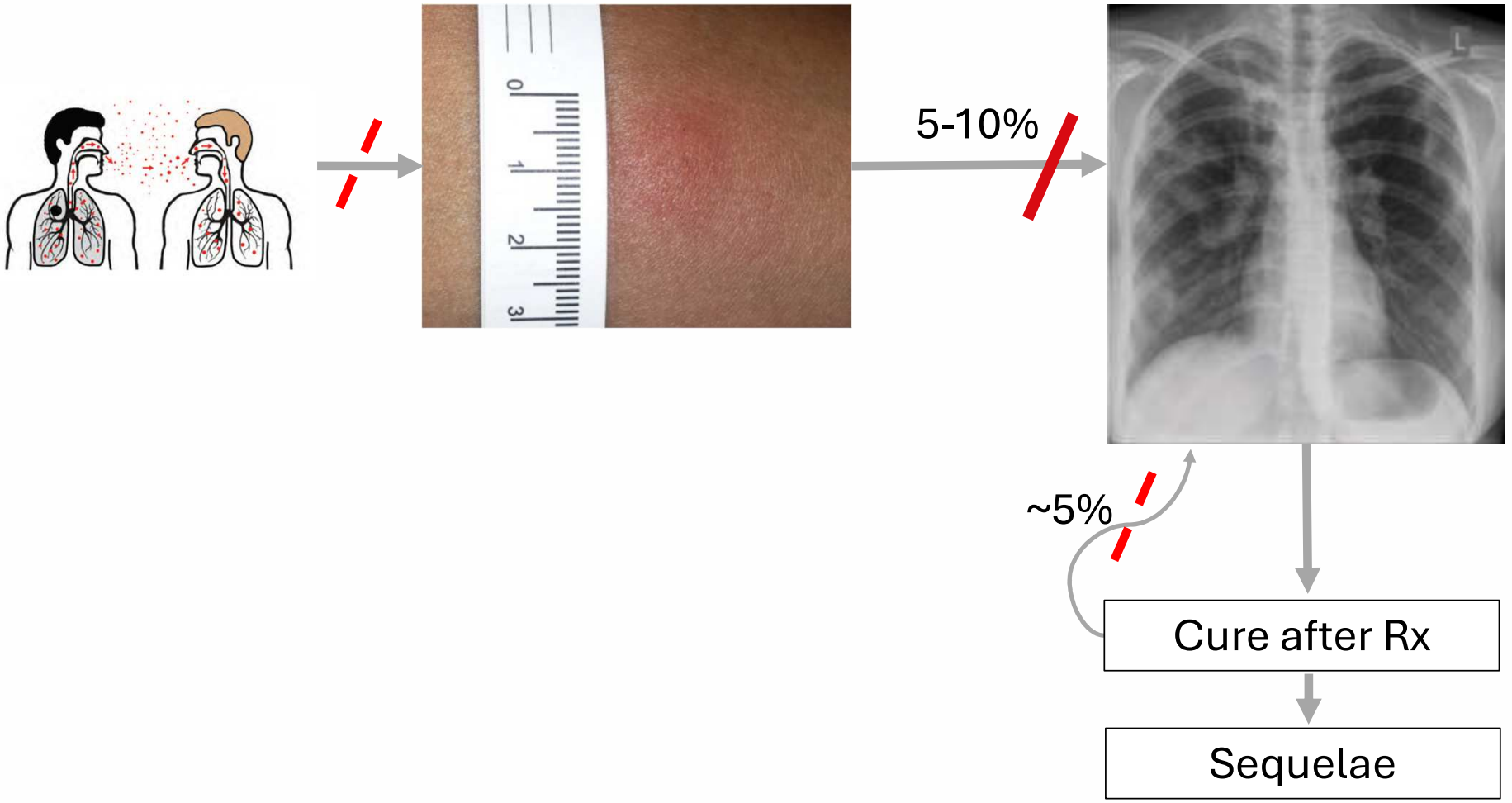
We need TB vaccines that prevent disease.



Global clinical TB vaccine pipeline: prophylaxis in adolescents and adults.

Phase 1	Phase 2A	Phase 2B	Phase 3
Ad5-105K Cansino, Etana	**BNT164a1 and BNT164b1** BioNTech, Gates Foundation	**MTBVAC** Biofabri, Univ Zaragosa, IAVI	**BCG as travel vaccine** HJF
H107e/CAF10b SSI	**ID93/GLA-SE (QTP101)** AAHI, Quratis, NIH		**GamTBvac** Gamaleya, MoH Russia
			M72/AS01$_{E-4}$ Gates MRI, GSK

1. Whole cell
2. Adjuvanted subunit
3. Viral vectored
4. mRNA

Modified from Stop TB Partnership. Only candidates in active clinical trials.

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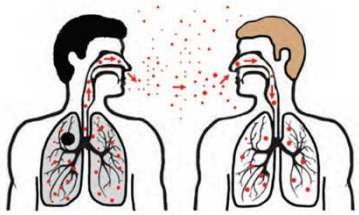
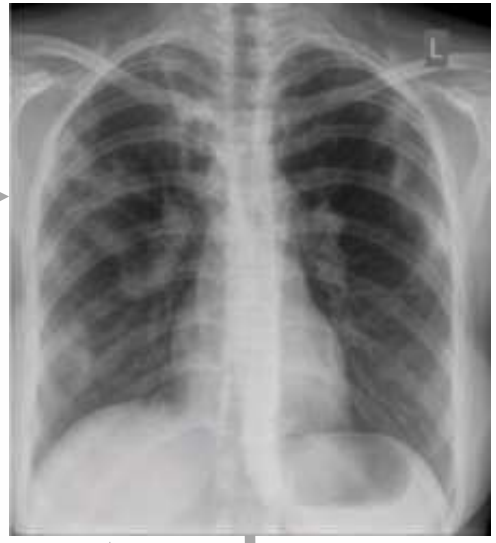
No-go decisions are common in product development.



5-10%



~5%

Cure after Rx

Sequelae

no PoI:
BCG revac
VPM1002
DAR901

no PoD:
VPM1002
Immuvac
MVA85A

earlier:
Aeras-402/404
H1,H4/IC31
TB/Flu-x
ChAd85A

no PoR:
H56/IC31
VPM1002

PoD but not practical:
SRL172
Vaccae

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Global clinical TB vaccine pipeline: prophylaxis in adolescents and adults.

Phase 1	Phase 2A	Phase 2B	Phase 3
Ad5-105K Cansino, Etana	**BNT164a1 and BNT164b1** BioNTech, Gates Foundation	**MTBVAC** Biofabri, Univ Zaragosa, IAVI	**BCG as travel vaccine** HJF
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			M72/AS01$_{E-4}$ Gates MRI, GSK

1. Most advanced and promising
2. Fast follower
3. Next generation

Modified from Stop TB Partnership.

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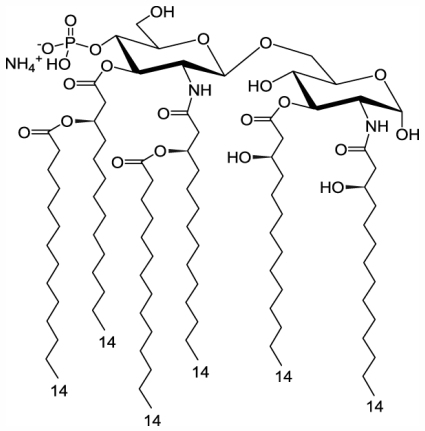
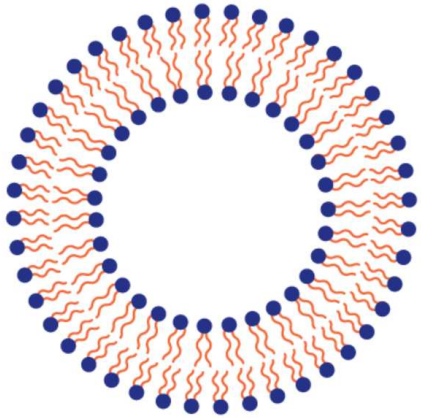
1. Most advanced and promising: M72/AS01$_{E-4}$.

1. Fusion protein

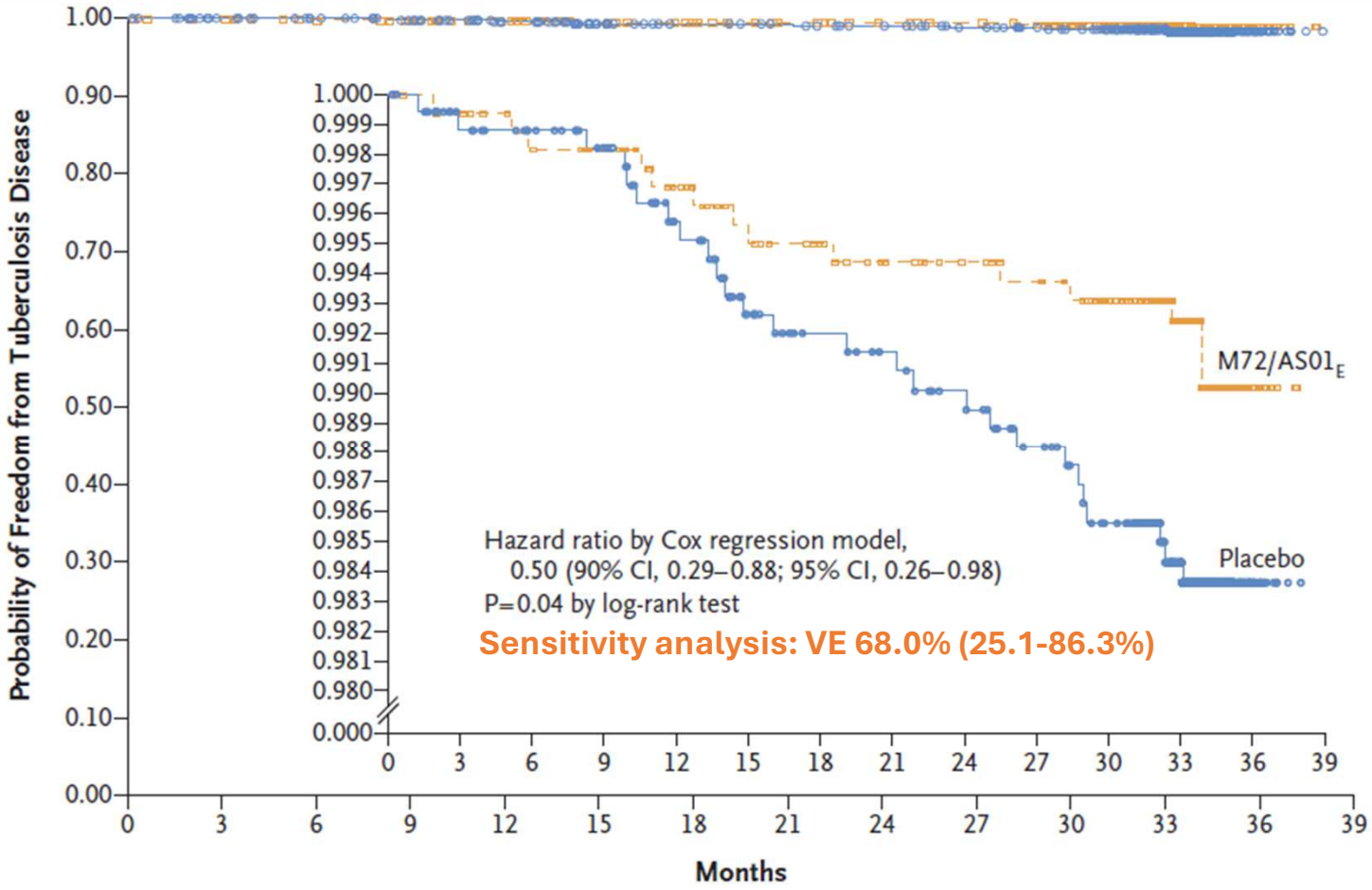
2. AS01E adjuvant: MPL, QS-21, liposome





BILL & MELINDA GATES MEDICAL RESEARCH INSTITUTE

Phase 2b: M72/AS01$_{E-4}$ protects against TB disease in QFT+ adults.



Tait, et al. N Engl J Med 2019: *n=3,575*.

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M72/AS01$_{E-4}$ phase 3 trial.

***Additional cohorts*: Safety and immunogenicity of IGRA negative and PLWH.**

- n=1,000 each.

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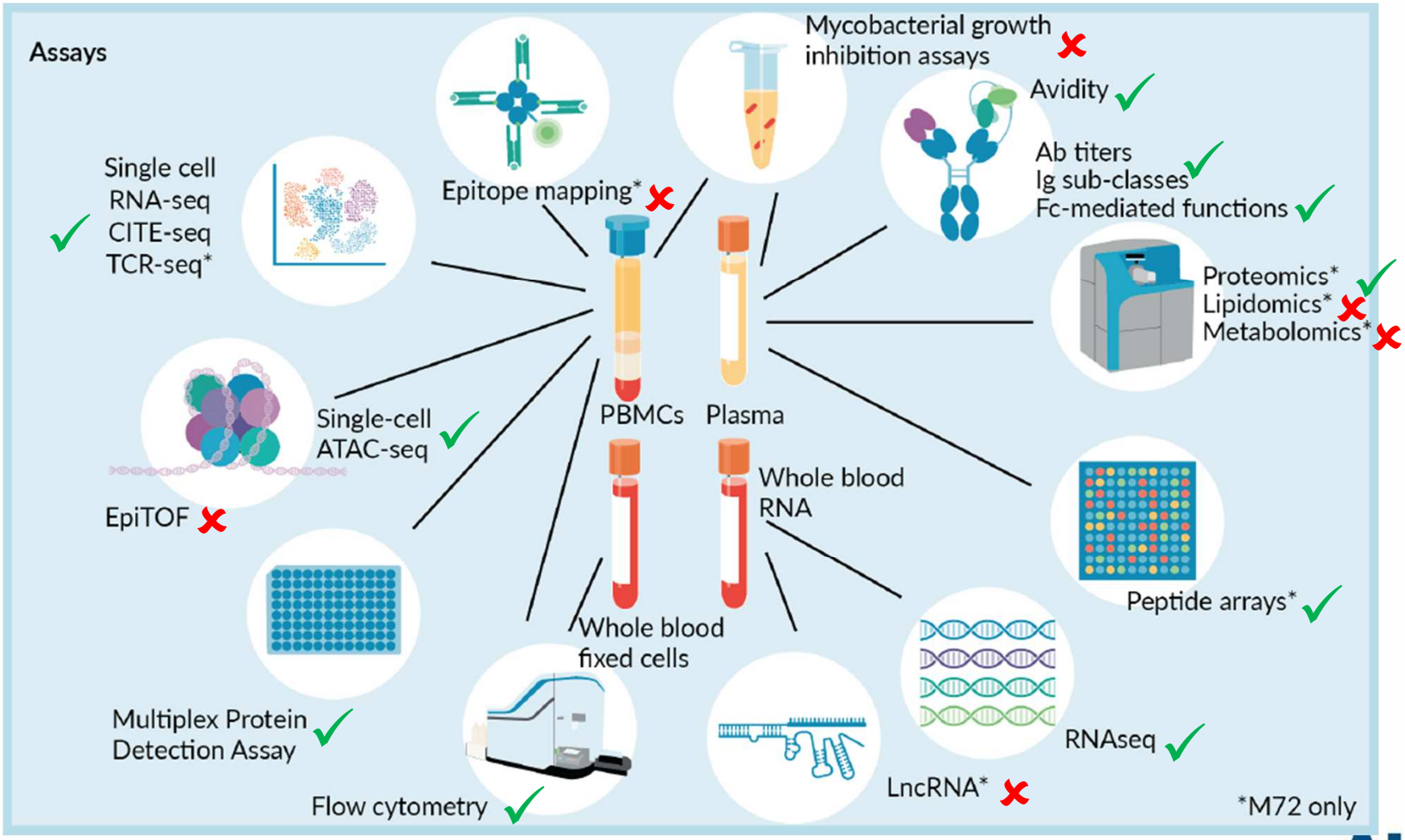
- **Implementation roadmaps** drafted for South Africa and Indonesia.
- **Consultation completed** with Zambia, Malawi and Kenya.
- **WHO TBVA** championing further efforts.

World Health Organization

Toward M72/AS01$_{E-4}$ induced correlates of protection.



Nemes and Fiore-Gartland, "*The quest for vaccine-induced immune correlates of protection against tuberculosis*". Vaccine Insights. 2022

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The Union

WORLD CONFERENCE ON LUNG HEALTH 2026

RIO DE JANEIRO
NOV 17-20

TBSCIENCE

TBScience 2026 Themes

Tuesday, 17th November 2026

Theme: Tuberculosis transmission: from identification to interruption

Interrupting tuberculosis transmission is central to ending the epidemic. This session will examine the dynamics of transmission and highlight advances in measuring and reconstructing transmission. Evidence-based strategies to interrupt transmission in high-burden settings will be explored.

Wednesday, 18th November 2026

Theme: Impact of heterogeneity among Mtb clinical isolates and lineages

Individual sputum isolates of Mtb, like global lineages of the pathogen, contain subpopulations with distinct traits and fitness. This session will explore the drivers and consequences of this heterogeneity. Potential impact on transmission, treatment outcomes, and vaccine efficacy will be addressed.

Thursday, 19th November 2026

Theme: Next-generation TB diagnostics and biomarker

This session will examine emerging diagnostics and biomarker approaches that enable earlier detection of tuberculosis and allow improved treatment monitoring and personalized care. Advances from discovery to implementation will be explored, with emphasis on impact in clinical and programmatic settings.

Friday, 20th November 2026

Expanding horizons: a One Health approach for mycobacterial diseases

This session will explore mycobacterial disease through a One Health lens, integrating human, animal, ecological, and environmental perspectives to better understand transmission, protection, persistence, and disease emergence across species and settings. Cross-disciplinary insights will be explored toward optimal intervention.

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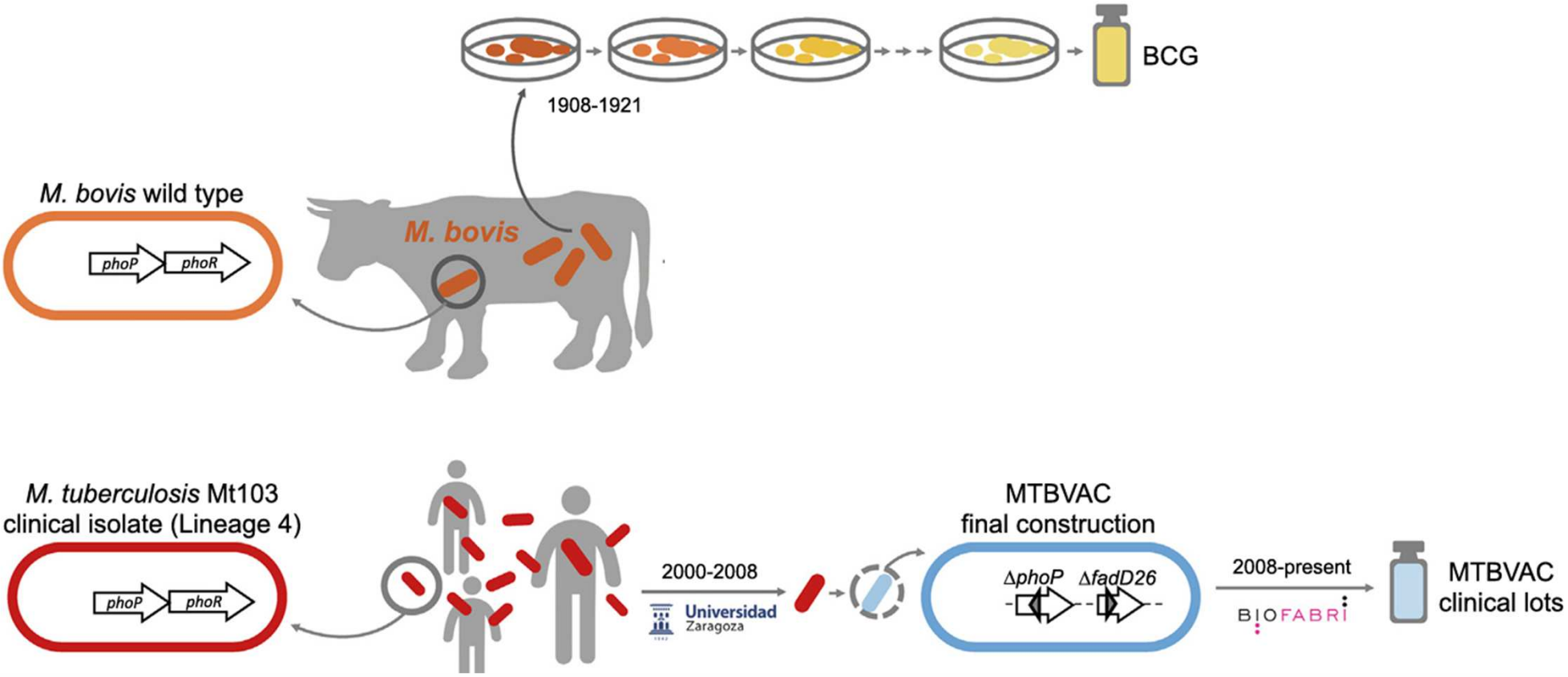
2. Fast follower: MTBVAC.



The vaccine is in a phase 2b trial in Africa and a phase 3 trial is planned for India.

Carlos Martin and colleagues.

IAVI C113 IMAGINE: Phase 2b study in adolescents and adults in Sub-Saharan Africa

Safety and proof-of-concept (POC) efficacy study for prevention of TB disease in IGRA+ African adults and adolescents [NCT06272812] **Status: ongoing; June 30th 93% enrolled**

Trial duration: 2025-2028

*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

Confidential

Co-funded by the European Union

Global Health EDCTP3

MTBVAC AVANTE Forward against TB

Critical issues for live attenuated whole cell vaccines, based on experience with BCG.

Safety in high HIV prevalence settings	• BCG may cause disease in immune compromised people • 1.8-2.1M people in South Africa do not know that they are living with HIV,
Effectiveness in high TB infection prevalence settings	• BCG does not seem to work when a persons has been sensitised by mycobacteria

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3. Next generation-1:

Lyophilized Thermostable Single-Vial ID93 + GLA-SE

ID93 Antigen — Four *M.tb.* Proteins

- **Rv1813** — hypoxia-associated
- **Rv2608** — PPE protein family
- **Rv3619 & Rv3620** — EsX family members

GLA-SE Adjuvant

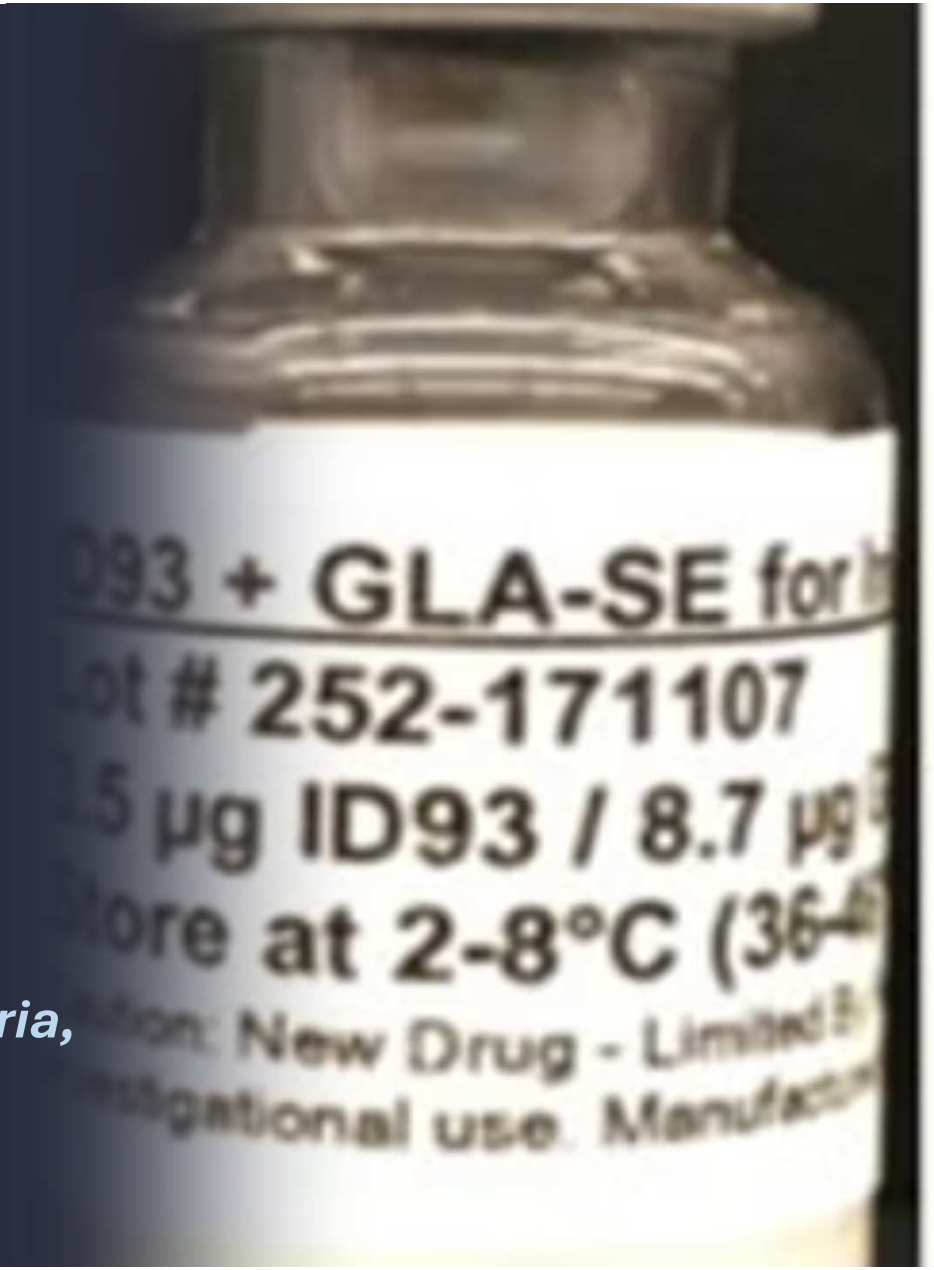
Synthetic TLR4 agonist in squalene-in-water emulsion. Stored at 2–8°C in the two-vial format.

Single-Vial Lyophilized Formulation

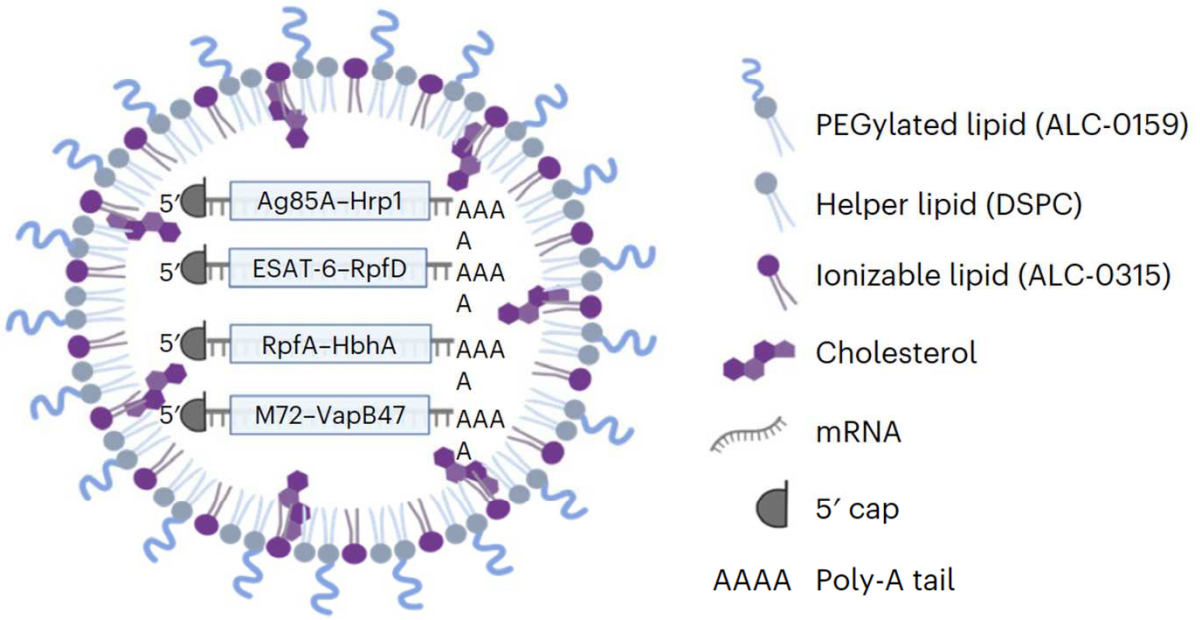
- ID93 + GLA-SE co-formulated in one vial
- cGMP manufactured; lyophilized cake
- Stable for **3 months at 37°C**

Phase 2a trial planned for South Africa and Nigeria, and elderly in Korea (QTP101).

aahi



3. Next generation-2: BNT164a1 and BNT164b1.



Antigen class: associated with…	Specific proteins encoded
"Latency"	VapB47 Hrp1
Reactivation	RpfA RpfD
Clinical disease	ESAT-6 Ag85A HbhA MTB32A MTB39A

Phase 2a trial ongoing in Southern Africa.

Agrawal et al. Nature Immunol 2025. BioNTech.

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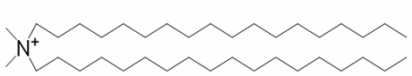
3. Next generation-3: H107e/CAF10b.

1. Fusion protein

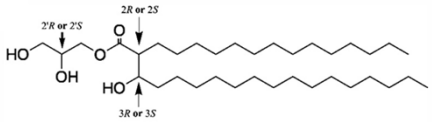
ESX-1 related

RD2/"Stress induced"/Ab targets

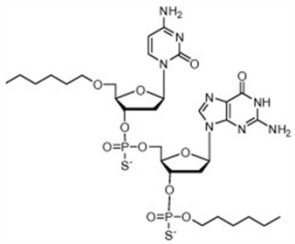
2. CAF10b adjuvant



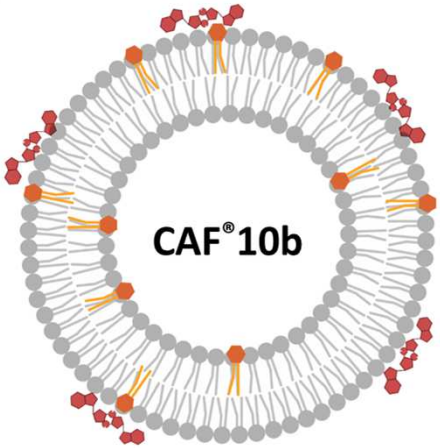
DDA



MMG



CpG2006



A phase 1/2a trial is planned, and a separate 2a trial in PLWH.

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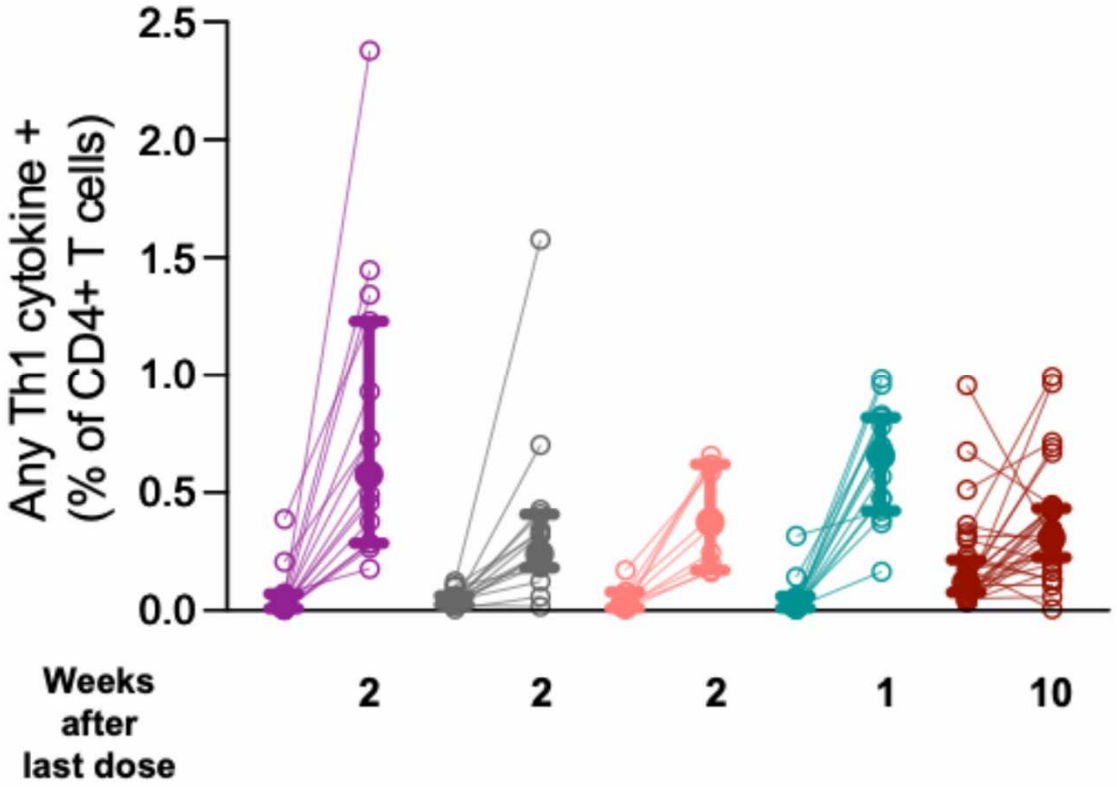
Data from humans (phase Ia) – WB-ICS (~12h stim).



H107e/CAF10b
20 µg H107e – Day 0+28 – n=15
8 Ag
nTB-01 (NCT06050356)

H56/IC31
5 µg H56 - Day 0+56 – n=15
3 Ag
C-035-456 (NCT01865487)

ID93/GLA-SE
10 µg ID93 - Day 0+28+112 – n=10
4 Ag
TBVPX-114 (NCT01927159)

M72/AS01$_E$
10 µg M72 – Day 0+30 – n=15
2 Ag
TB010 (NCT00950612)

BCG (revaccination)
2-8x10^5 CFU Day 0 – n=28
Whole cell inactivated vaccine
C-040-404 (NCT02075203)

IGRA-
Adults,
Peptide pool stim

IGRA-
Adolescents
BCG stim

25 YEARS OF TB RESEARCH | satvi TOWARDS A WORLD WITHOUT TB

STATENS SERUM INSTITUT

3. Next generation-4: Ad5-105K.

Generic Name: Inhaled Tuberculosis Vaccine (Adenovirus Type 5 Vector), Ad5-105K("*ADTB*")

Active Ingredient: A replication-deficient human adenovirus serotype 5 expressing the Mtb antigen 105K fusion protein (*Ag85A, Mtb32A and Mtb39A*)

Specification: 0.5 mL per vial

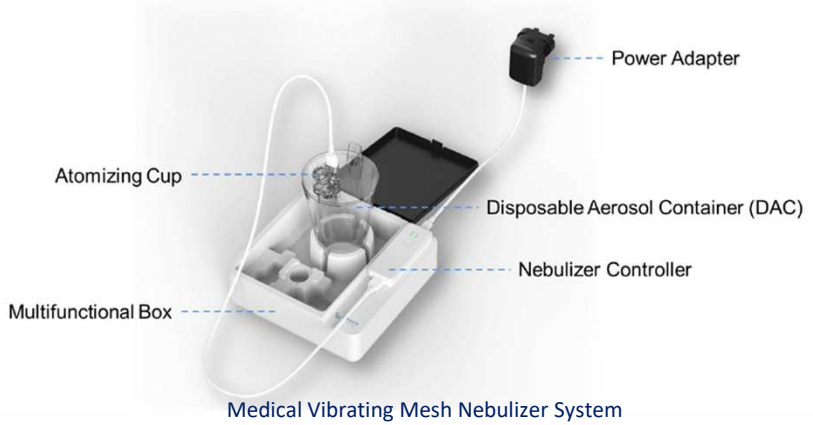
Shelf life: Tentatively 24 months

Dosage: 0.1 mL or 0.2 mL (1×10^8VP per 0.1 mL)

Storage: Store and transport at 2-8°C

Manufacturer: CanSino Biologics Inc.

Inhalation Delivery System



Medical Vibrating Mesh Nebulizer System

Inhalation of Nebulized Vaccine

Phase 1 trial completed in Indonesia.

康希诺生物
CanSinoBIO

Phase 1 Clinical Trial - Interim safety results

	ADTB Low (N=12) n (%)	ADTB High (N=12) n (%)	Placebo (N=12) n (%)	Overall (N=36)
Any Vaccine-related AEs within 28 days	**8 (66.67)**	**5 (41.67)**	**3 (25.00)**	**16 (44.44)**
Grade 1	**5(41.7)**	**5(41.7)**	**3(25.0)**	**13(36.1)**
Grade 2	**3(25.0)**	**0**	**0**	**3(8.3)**
≥ Grade 3	**0**	**0**	**0**	**0**
Fatigue	4 (33.33)	1 (8.33)	1 (8.33)	6 (16.67)
Dry mouth	4 (33.33)	1 (8.33)	1 (8.33)	6 (16.67)
Headache	2 (16.67)	0	2 (16.67)	4 (11.11)
Oropharyngeal pain	1 (8.33)	1 (8.33)	0	2 (5.56)
Aphthous ulcer	1 (8.33)	0	0	1 (2.78)
Nausea	1 (8.33)	0	0	1 (2.78)
Vomiting	1 (8.33)	0	0	1 (2.78)
Hypoaesthesia	1 (8.33)	0	0	1 (2.78)
Mass	1 (8.33)	0	0	1 (2.78)
Arthralgia	1 (8.33)	0	0	1 (2.78)
Muscular weakness	1 (8.33)	0	0	1 (2.78)
Erythema	1 (8.33)	0	0	1 (2.78)
Rash erythematous	1 (8.33)	0	0	1 (2.78)
Pain	0	1 (8.33)	0	1 (2.78)
Rhinorrhoea	0	1 (8.33)	0	1 (2.78)

No reports of Grade 3 and above AE or SAE
Safety profiles were comparable among the three groups

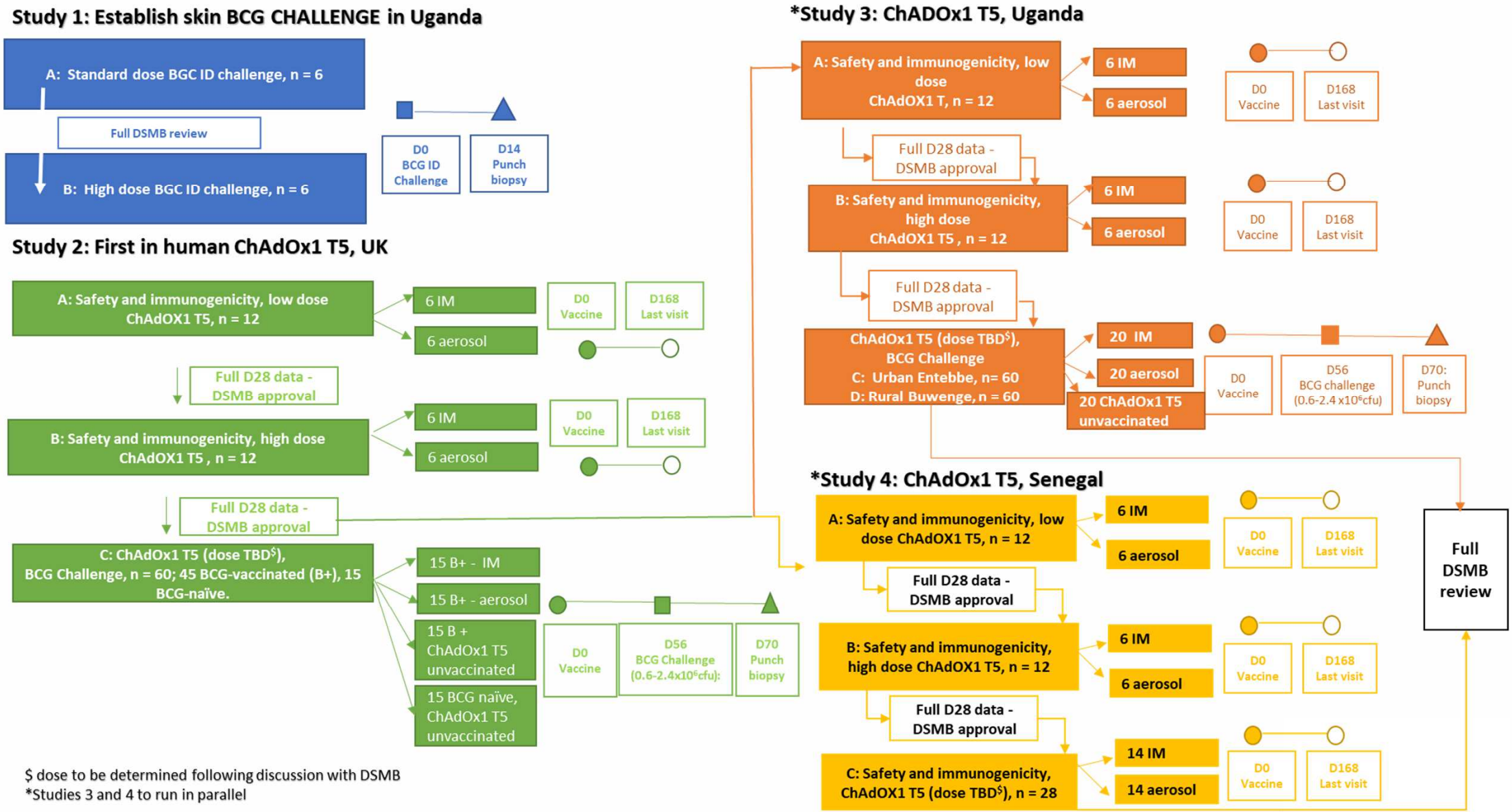
康希诺生物
CanSinoBIO

3. Next generation-5: **ChAdOx1-T5.**

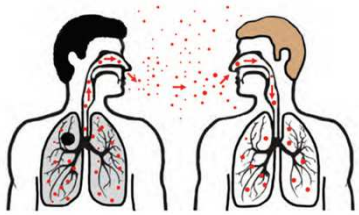
- Recombinant chimpanzee adenovirus (ChAdOx1) expressing 5 mycobacterial antigens:

- Each antigen protective when delivered alone
- Esx-5a complex is composed of PE8, PPE15, esxI, esxJ

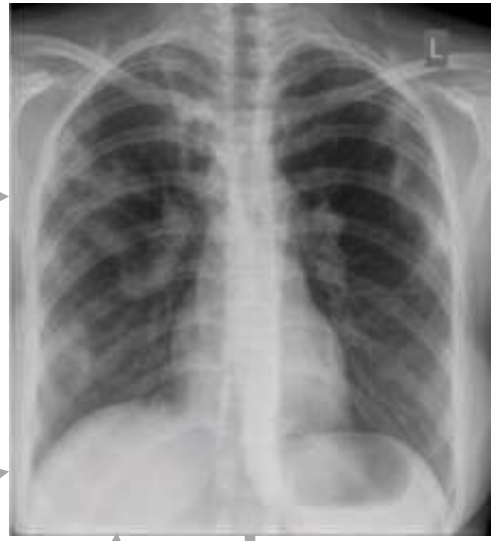
UNIVERSITY OF OXFORD


Study 1: Establish skin BCG CHALLENGE in Uganda
A: Standard dose BGC ID challenge, n = 6
Full DSMB review
B: High dose BGC ID challenge, n = 6
D0 BCG ID Challenge
D14 Punch biopsy
Study 2: First in human ChAdOx1 T5, UK
A: Safety and immunogenicity, low dose ChAdOX1 T5, n = 12
6 IM
6 aerosol
D0 Vaccine
D168 Last visit
Full D28 data - DSMB approval
B: Safety and immunogenicity, high dose ChAdOX1 T5 , n = 12
6 IM
6 aerosol
D0 Vaccine
D168 Last visit
Full D28 data - DSMB approval
C: ChAdOx1 T5 (dose TBD$), BCG Challenge, n = 60; 45 BCG-vaccinated (B+), 15 BCG-naïve.
15 B+ - IM
15 B+ - aerosol
15 B + ChAdOx1 T5 unvaccinated
15 BCG naïve, ChAdOx1 T5 unvaccinated
D0 Vaccine
D56 BCG Challenge (0.6-2.4x10⁶cfu):
D70 Punch biopsy
$ dose to be determined following discussion with DSMB
*Studies 3 and 4 to run in parallel
*Study 3: ChADOx1 T5, Uganda
A: Safety and immunogenicity, low dose ChAdOX1 T, n = 12
6 IM
6 aerosol
D0 Vaccine
D168 Last visit
Full D28 data - DSMB approval
B: Safety and immunogenicity, high dose ChAdOX1 T5 , n = 12
6 IM
6 aerosol
D0 Vaccine
D168 Last visit
Full D28 data - DSMB approval
ChAdOx1 T5 (dose TBD$), BCG Challenge
C: Urban Entebbe, n= 60
D: Rural Buwenge, n = 60
20 IM
20 aerosol
20 ChAdOx1 T5 unvaccinated
D0 Vaccine
D56 BCG challenge (0.6-2.4 x10⁶cfu)
D70: Punch biopsy
*Study 4: ChAdOx1 T5, Senegal
A: Safety and immunogenicity, low dose ChAdOX1 T5, n = 12
6 IM
6 aerosol
D0 Vaccine
D168 Last visit
Full D28 data - DSMB approval
B: Safety and immunogenicity, high dose ChAdOX1 T5, n = 12
6 IM
6 aerosol
D0 Vaccine
D168 Last visit
Full D28 data - DSMB approval
C: Safety and immunogenicity, ChAdOX1 T5 (dose TBD$), n = 28
14 IM
14 aerosol
D0 Vaccine
D168 Last visit
Full DSMB review

New directions: preventing asymptomatic TB?



5-10%



Asymptomatic TB

~5%

Self-cure

Cure after Rx

Sequelae

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Conclusions

1. We need vaccines that **prevent TB in adolescents and adults**.
2. **M72/AS01$_{E-4}$** is in a phase 3 trial, while **MTBVAC** is a fast follower.
3. A **next generation** of vaccines is emerging, based on basic science advances and resulting in use of more optimal antigens, novel platforms and optimal adjuvants.
4. There is an urgent need to **populate** the clinical TB vaccine pipeline from the left.
5. It is critical to plan for **implementation** now.

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