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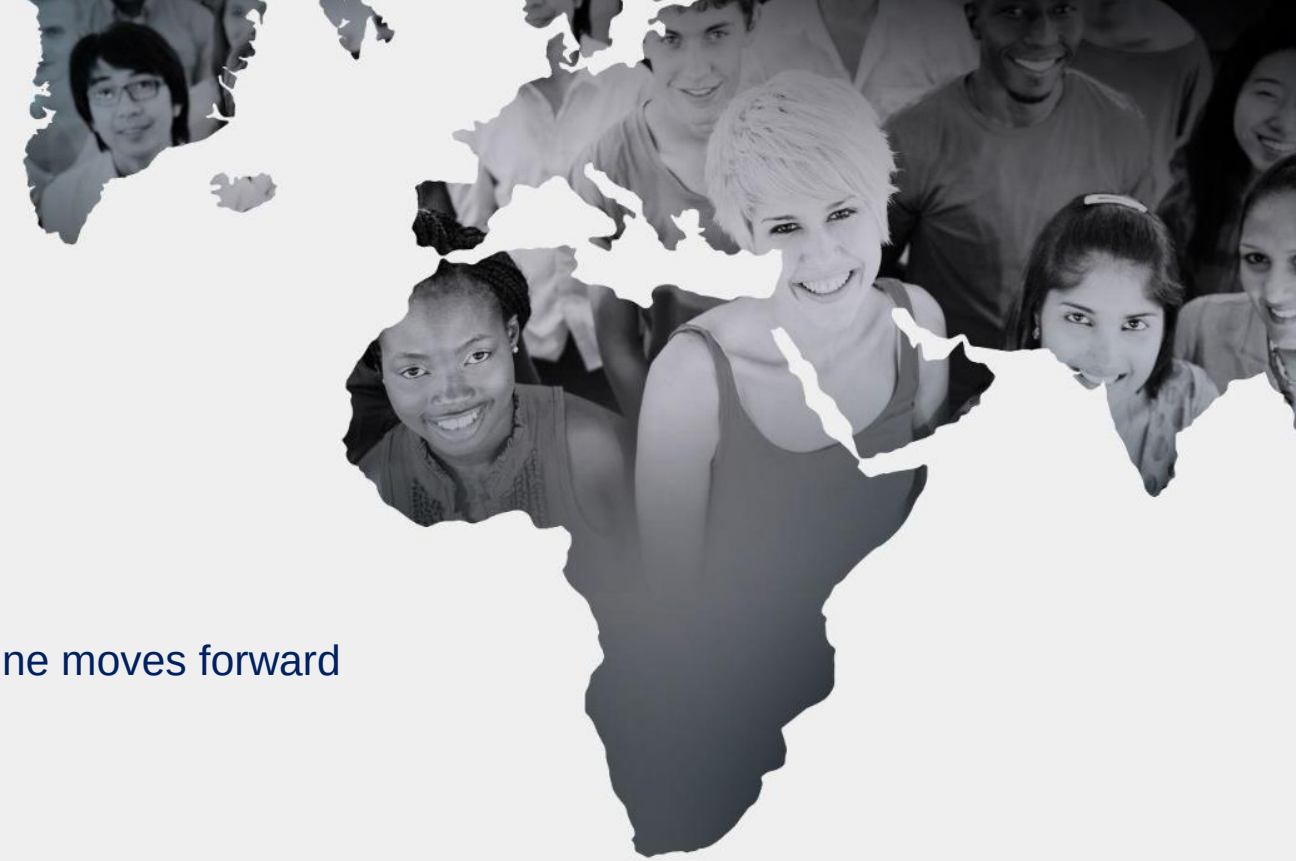

VPM1002

A next generation BCG vaccine moves forward

RePORT International Annual Meeting
6th Sept 2023

VPM1002-Product Profile and Mechanism of Action

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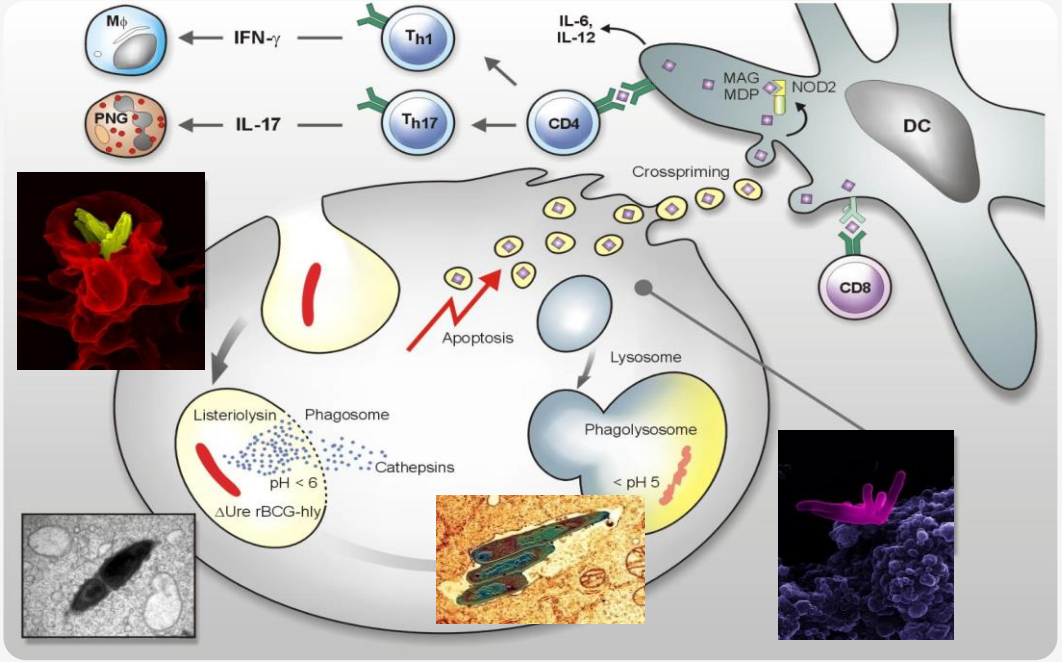
- Parental Strain: BCG subtype Prague
- Genetic Modification: Listeriolysin gene inserted into the bacterial genome (Urease C gene)
- Induction of apoptosis and autophagy lead to enhanced cross-presentation and better immune activation.
- Induction of apoptosis results in shorter persistence of VPM1002 in the body, which makes the vaccine safer than BCG.



VPM1002- Clinical Development

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R&D | 2004/05 | 2006 | 2007 | 2008/09 | 2010/11 | 2012/13 | 2014-17 | 2018/19 | 2020-

In-licensing | GMP material | Non-clinical | FiH | Phase Ib | Phase IIa | Phase II | Phase III



priMe

Phase II/III — TB post-exposure

Phase III — TB Household contacts

Phase III — TB Healthcare professionals

Phase I/II — VPM1002BC NMIBC

Phase III — COVID-19 risk-groups

rBCG (VPM1002) Development Program

- **TB**
  - *prime Vaccine*
  - *post exposure*
  - *House Hold Contact*
- **Prevention of respiratory tract infections**
  - *People at risk (HCP, elderly)*
- **Bladder cancer**
  - *NMIBC*

Phase Ia, Phase Ib, Phase IIa, Phase II, Phase III (ongoing) → **~7000 participants exposed to rBCG including infants**

Phase II/III (ongoing), Phase III (ongoing) → **~7000 participants exposed to rBCG including infants**

2 x Phase III → **~4000 participants exposed to rBCG**

Phase II → **~40 participants exposed to rBCG (intravesically)**

efficacy:
- **immunogen (confirmative trials ongoing)**

safety and tolerability:
- **at least as safe as BCG**

efficacy shown for:
- **prevention of respiratory diseases**
- **treatment of NMIBC**

safety: no safety concerns

2015-2018

phase I/II NMIBC

* Pictures are for representation purpose only

VPM1002- Clinical Development

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Contents lists available at SciVerse ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Safety and immunogenicity of the recombinant BCG vaccine VPM1002 in a phase 1 open-label randomized clinical trial

Leander Grode[a,1], Christian A. Ganoza[b,1], Christiane Brohm[a,1], January Weiner 3rd[b], Bernd Eisele[a], Stefan H.E. Kaufmann[b,*]

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ARTICLE INFO

Article history:
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Received in revised form

ABSTRACT

Background: Current vaccination using *Mycobacterium bovis* bacillus Calmette-Guérin (BCG), fails to prevent pulmonary tuberculosis (TB). New vaccination strategies are essential for reducing the global incidence of TB. We assessed the safety and immunogenicity of VPM1002, a recombinant BCG vaccine

ONCOIMMUNOLOGY
2020, VOL. 9, NO. 01, e1748981 (8 pages)
https://doi.org/10.1080/2162402X.2020.1748981

Taylor & Francis
Taylor & Francis Group

BRIEF REPORT

OPEN ACCESS Check for updates

Results of the phase I open label clinical trial SAKK 06/14 assessing safety of intravesical instillation of VPM1002BC, a recombinant mycobacterium Bacillus Calmette Guérin (BCG), in patients with non-muscle invasive bladder cancer and previous failure of conventional BCG therapy

Cyrill A. Rentsch[a], Piet Bosshard[a,b*], Grégoire Mayor[c], Malte Rieken[a], Heike Püschel[a], Grégory Wirth[c], Richard Cathomas[d], Gerald P. Parzmair[e], Leander Grode[e], Bernd Eisele[e], Hitt Sharma[f], Manish Gupta[f], Sunil Gairola[f], Umesh Shaligram[f], Daniel Goldenberger[a], François Spertini[h], Régine Audran[h], Milica Enoiu[i], Simona Berardi[g], Stefanie Hayoz[g], and Andreas Wicki[j] for the Swiss Group for Clinical Cancer Research (SAKK)

[a]Department of Urology, University Hospital Basel, University of Basel, Basel, Switzerland; [b]Department of Urology, University Hospital Bern, University of Bern, Bern, Switzerland; [c]Department of Urology, University Hospital Geneva, University of Geneva, Geneva, Switzerland; [d]Department of Oncology, Cantonal Hospital Chur, Chur, Switzerland; [e]Vakzine Projekt Management GmbH, Hannover, Germany; [f]Serum Institute of India Pvt. Ltd., Pune, India; [g]Department of Clinical Bacteriology & Mycology, University Hospital Basel, University of Basel, Basel, Switzerland; [h]Division of Immunology and Allergy, Lausanne University Hospital, Lausanne, Switzerland; [i]SAKK Coordinating Center, Bern, Switzerland; [j]Department of Oncology, University Hospital Basel, University of Basel, Switzerland

THE LANCET
Infectious Diseases

Volume 22, Issue 10, October 2022, Pages 1472-1483

Articles

Safety and immunogenicity of VPM1002 versus BCG in South African newborn babies: a randomised, phase 2 non-inferiority double-blind controlled trial

Prof Mark F Cotton MD [a]*, Prof Shabir A Madhi PhD [b c d], Angelique K Luabeya MD [a]*, Michele Tameris MBChB [a]*, Anneke C Hesseling PhD [f], Justin Shenje MBChB [a]*, Elisma Schoeman MD [a]*, Prof Mark Hatherill MD [c e]*, Sajjad Desai MD [g], Dhananjay Kapse MD [g], Sina Brückner PhD [h], Anthonet Koen MBChB [b c d], Lisa Jose MBChB [b c d], Andrew Moultrie BSc [b c d], Sutika Bhikha MBChB [b c d], Prof Gerhard Walzl PhD [i], Andrea Gutschmidt MSc [i], Leigh A Kotze PhD [i], Devon L Allies ND [i], Prof Andre G Loxton PhD [i]…Prasad S Kulkarni MD [g]

VPM1002 as Prophylaxis Against Severe Respiratory Tract Infections Including Coronavirus Disease 2019 in the Elderly: A Phase 3 Randomized, Double-Blind, Placebo-Controlled, Multicenter Clinical Study

FREE

Alexandra M Blossey, Sina Brückner, Marcus May, Gerald P Parzmair, Hitt Sharma, Umesh Shaligram, Leander Grode, Stefan H E Kaufmann, Mihai G Netea, Christoph Schindler Author Notes

Clinical Infectious Diseases, Volume 76, Issue 7, 1 April 2023, Pages 1304–1310,
https://doi.org/10.1093/cid/ciac881

Published: 11 November 2022 **Article history**

Clinical Development- PriMe Trial

Study title: A multicenter, phase III, double-blind, randomized, active-controlled study to evaluate the efficacy and safety of VPM1002 vs BCG in prevention of Mycobacterium tuberculosis infection in newborn infants

[redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]

[redacted]

Clinical Development- Prevention of Recurrence

Study title: Phase II/III Double-blind, Randomized, Placebo Controlled Study to Evaluate the Efficacy And Safety Of VPM1002 in the Prevention of Tuberculosis (TB) Recurrence In Pulmonary TB Patients after Successful TB Treatment

[redacted]

Clinical Development- Household contact

Study title: A Phase III, Randomized, Double-blind, Three arm Placebo controlled Trial to Evaluate the Efficacy and Safety of two vaccines VPM1002 and Immuvac(Mw) in Preventing Tuberculosis (TB) in Healthy Household Contacts of Newly Diagnosed Sputum Positive Pulmonary TB Patients.

[redacted]

Goal and Strategy for TB elimination

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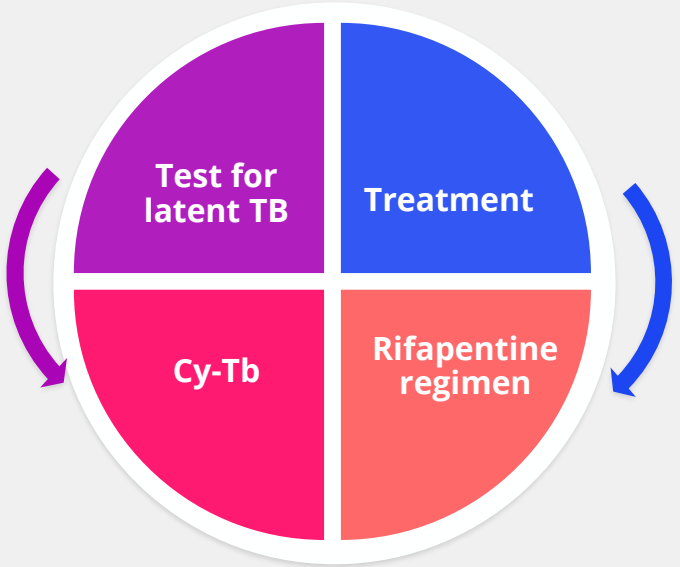
Strategy towards **"End TB"** from the World

Complete Solution – State of Art

- Detect –Infection (Cy-Tb)
- Treat –Infection (Isoniazid/Rifapentine*)
- Prevent–Infection/Recurrence
  (rBCG Vaccine VPM1002)

*Available from other manufacturers in India

An important step towards a TB free world



Prevention rBCG Vaccine

Cy-Tb is Mtb-specific

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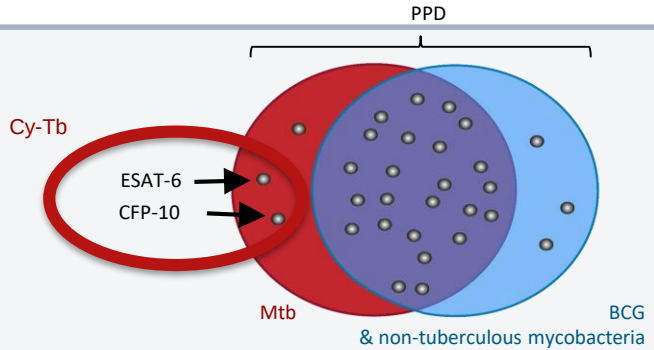
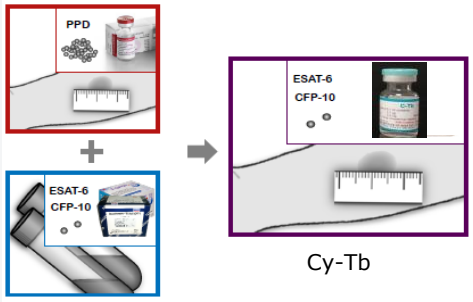
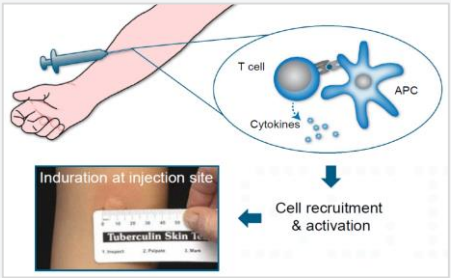
- PPD contains a crude mix of antigens present in both Mtb, BCG and non-tuberculous mycobacteria
- Cy-Tb & IGRAs contain purified ESAT-6 and CFP-10
- ESAT-6 and CFP-10 are only present in Mtb
- Cy-Tb combines the simplicity of the skin test with the diagnostic accuracy of the IGRA tests

- Induration reading method for Cy-Tb is **similar to PPD** after 48 h to 72 h of injection.
- Universal **5 mm** cut off has been established for Cy-Tb







Ecosystem Solution at Each Step

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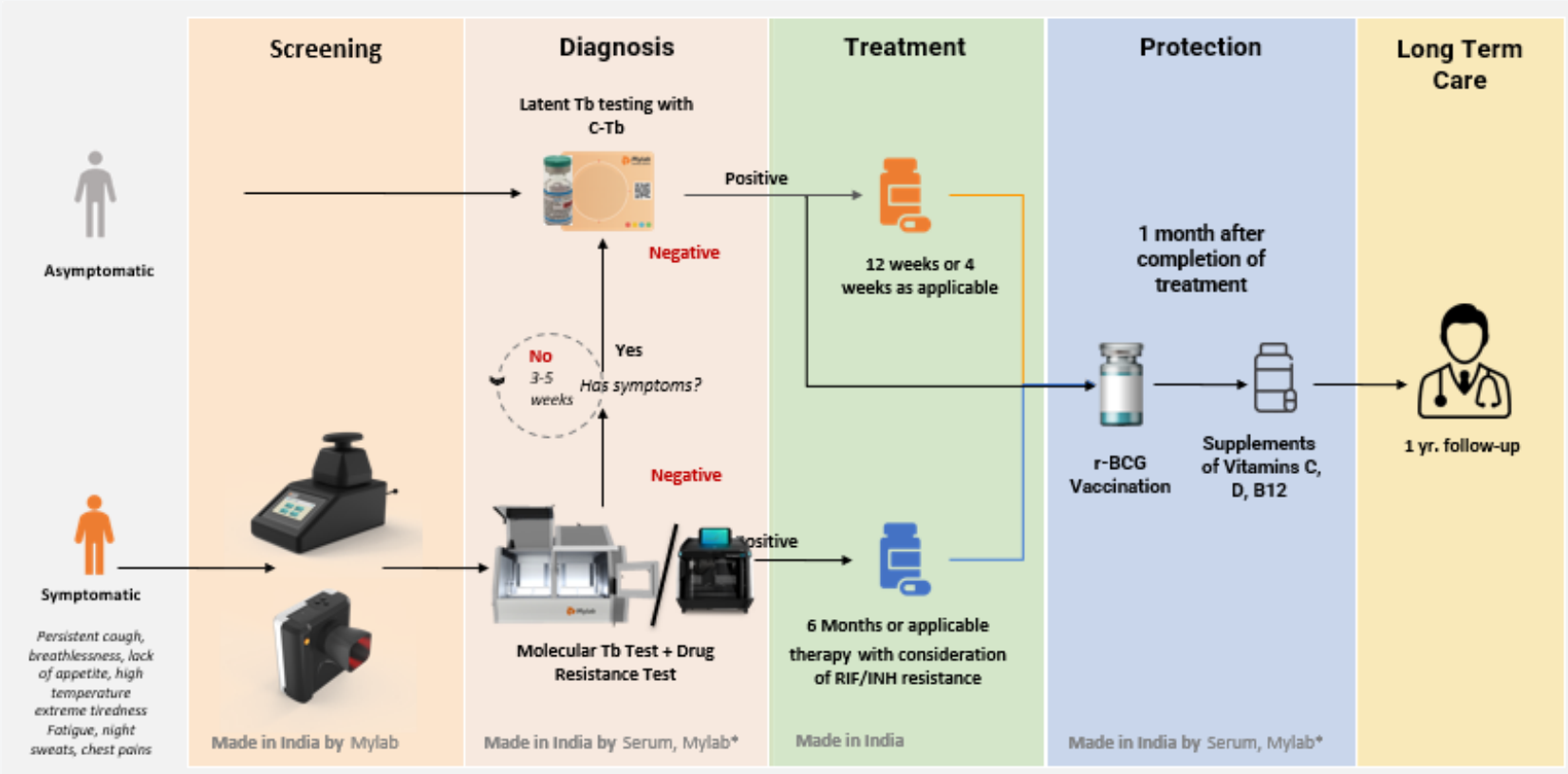
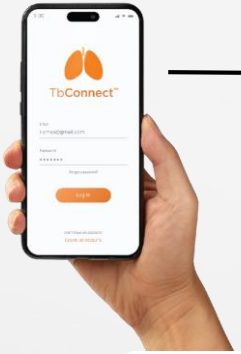
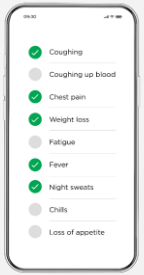


ONE DAY. ONE VILLAGE. ZERO TB

Registration on TBConnect



Symptoms & Vulnerability Check



X ray Screening

Active TB & MDR Testing

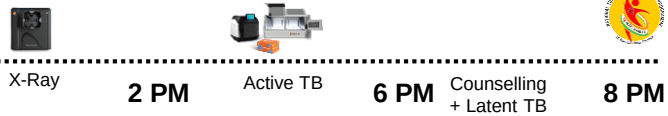
Reports on Nikshay

Cy-Tb for Household Contacts of Positive

Prep — **DAY 01** — **Post**

Before Camp, Community Health Worker:

- Registers Patients
- Checks Symptoms
- Vulnerability Mapping



Latent Testing

- Community worker to do Cy-TB testing for household contacts

LAB TECHNICIAN | PATIENTS | HEALTHCARE WORKER | HOUSEHOOLD CONTACTS

THE FUNNEL

1000 people

Symptoms & Vulnerability Check

15-20%

150-200 people

X-Ray Screening

10-15%

30 people

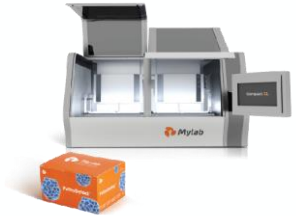
Active TB & MDR

0.3%

5-10 HHC

Cy-TB
(4+ HHC)

X-ray Screening yields 10% positive in screening

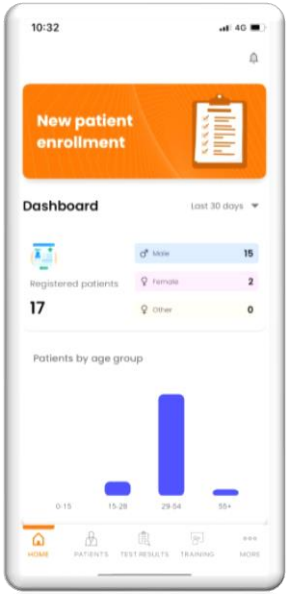


MDR-RIF INH usually results in 3-7 positive per 1000 population

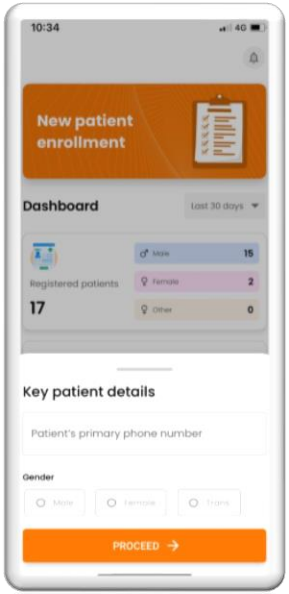
Cy-Tb usually results in 30% positive in general population

TBCONNECT COMPLETE DIGITAL WORKFLOW SOLUTION

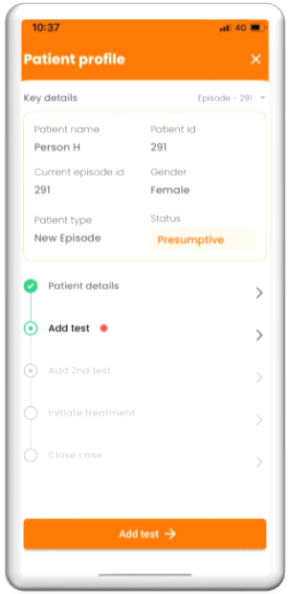
Dashboard



Patient Registration

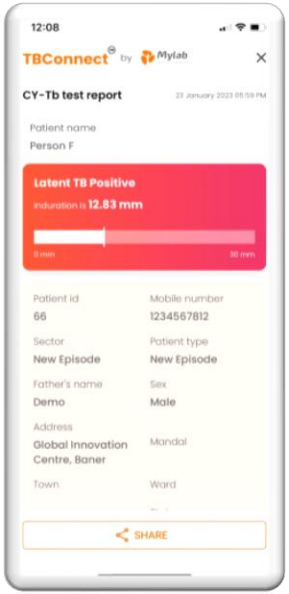


Patient Flow & Workflow



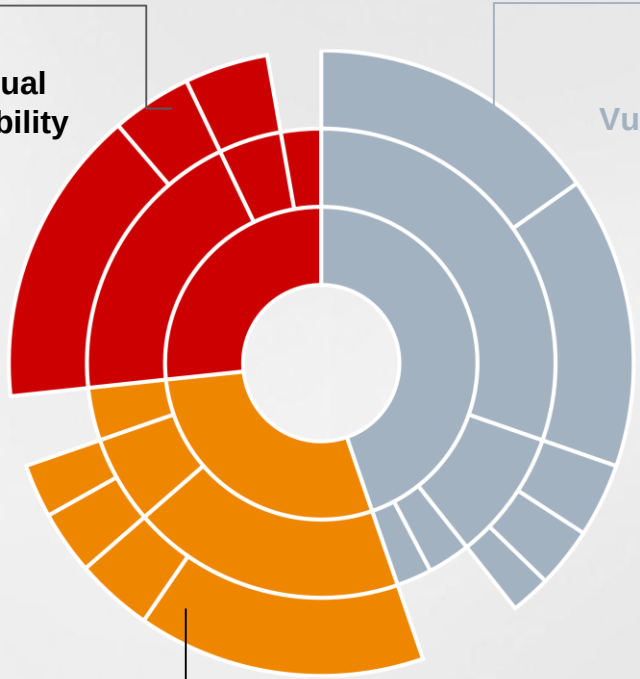
Automated Interpretation

Informative Reports



A UNIQUE MODEL FOR VULNERABILITY MAPPING

- Household TB Contact
- Diabetes
- Smoking
- Past TB
- Liver/kidney issues
- Tribal
- Healthcare Worker
- Mine worker
- Slum Dwelling
- Migrant
- Geo TB prevalence
- Geo TB Incidence
- Coastal Residence
- Humidity in Region
- Other



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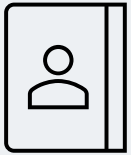
HELPS YOU IDENTIFY THE MOST LIKELY TO BE POSITIVE

Know Your Impact. Live.

Live Dashboard
(updated every 15 min)

- Live dashboard with details on number total People Screened by Village, Positive Negative ratios, etc. with option to deep dive

Executive Reports
(every week)



- Email Reports with Key statistics on progress of the programs

Impact Reports
(every quarter)

- Quarterly impact reports with estimates of lives saved, families screened, future cases prevented, DALY saved.

PR Briefings
(per area)

- PR briefings in local language and support in local PR to spread the good word.

Acknowledgements

SIIPL sincerely acknowledges all the help provided by Govt. of India and several national and international organizations like DCGI, DBT, ICMR, NIH, RePORT and others.

स्वास्थ्य एवं परिवार कल्याण मंत्रालय
MINISTRY OF HEALTH AND FAMILY WELFARE
सत्यमेव जयते

भारत सरकार GOVERNMENT OF INDIA
विज्ञान और प्रौद्योगिकी मंत्रालय MINISTRY OF SCIENCE AND TECHNOLOGY
जैवप्रौद्योगिकी विभाग
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RePORT INTERNATIONAL

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Thank you!

1966

SIIPL Founded in Pune, India.

>1.7 B

doses/year = world's largest vaccine manufacturer

170

countries use SIIPL vaccines

60%

of children are protected by SIIPL vaccines

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