RePORT India Consortium

Regional **P**rospective **O**bservational **R**esearch for **T**B

Amita Gupta MD, MHS

- RePORT India US Chair and RePORT International EC Member
- US PI of CTRIUMPH cohort
- Associate Professor of Medicine and International Health
- Deputy Director, Center for Clinical Global Health Education
- John Hopkins University, USA

- **RePORT International Meeting Durban, South Africa, July 15, 2016**

RePORT India Consortium

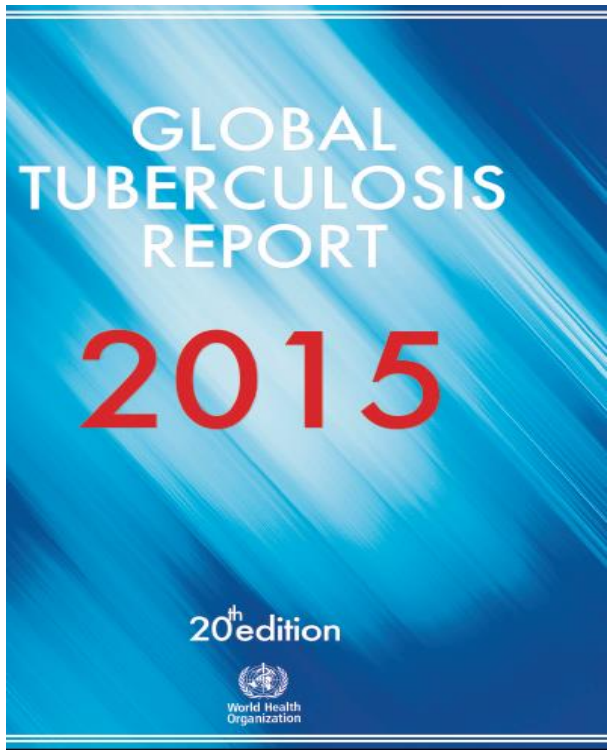
Regional Prospective Observational Research for Tuberculosis

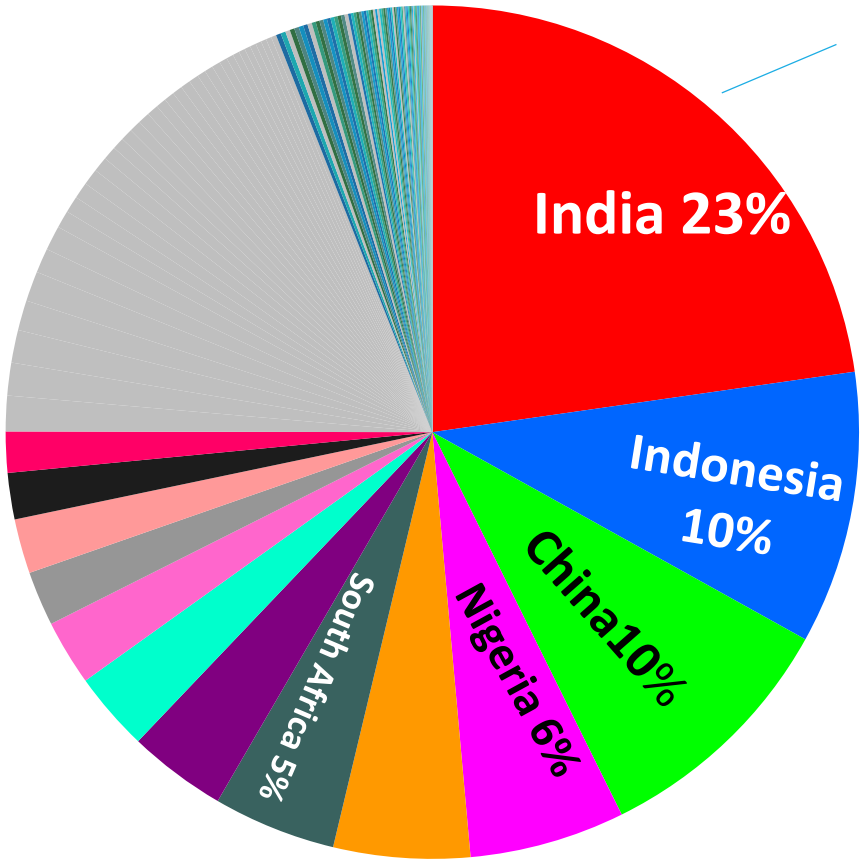
IndoUS TB Research Collaboration

Why RePORT India Consortium?

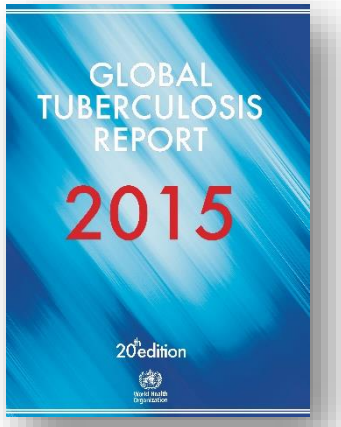
- Globally- India highest TB burden and many different comorbidities and drivers of TB
- TB research siloed and clinical research and basic research efforts not well coordinated
- Large and collaborative research = better and faster results!

India ranks one in burden of TB: 23% of all cases



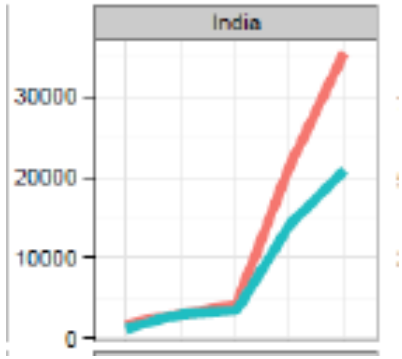


2.2 million of 9.6 million global TB cases



India - TB Burden

	Estimated Incidence	Estimated # Deaths
All forms TB	2.2 million (2.0 -2.3 million) (Rate 167)	0.22 million* (0.15 -0.25 million)
HIV-associated TB	0.11 million (0.09-0.12 million)	390,000
MDR TB	71,000 amongst notified cases	190,000



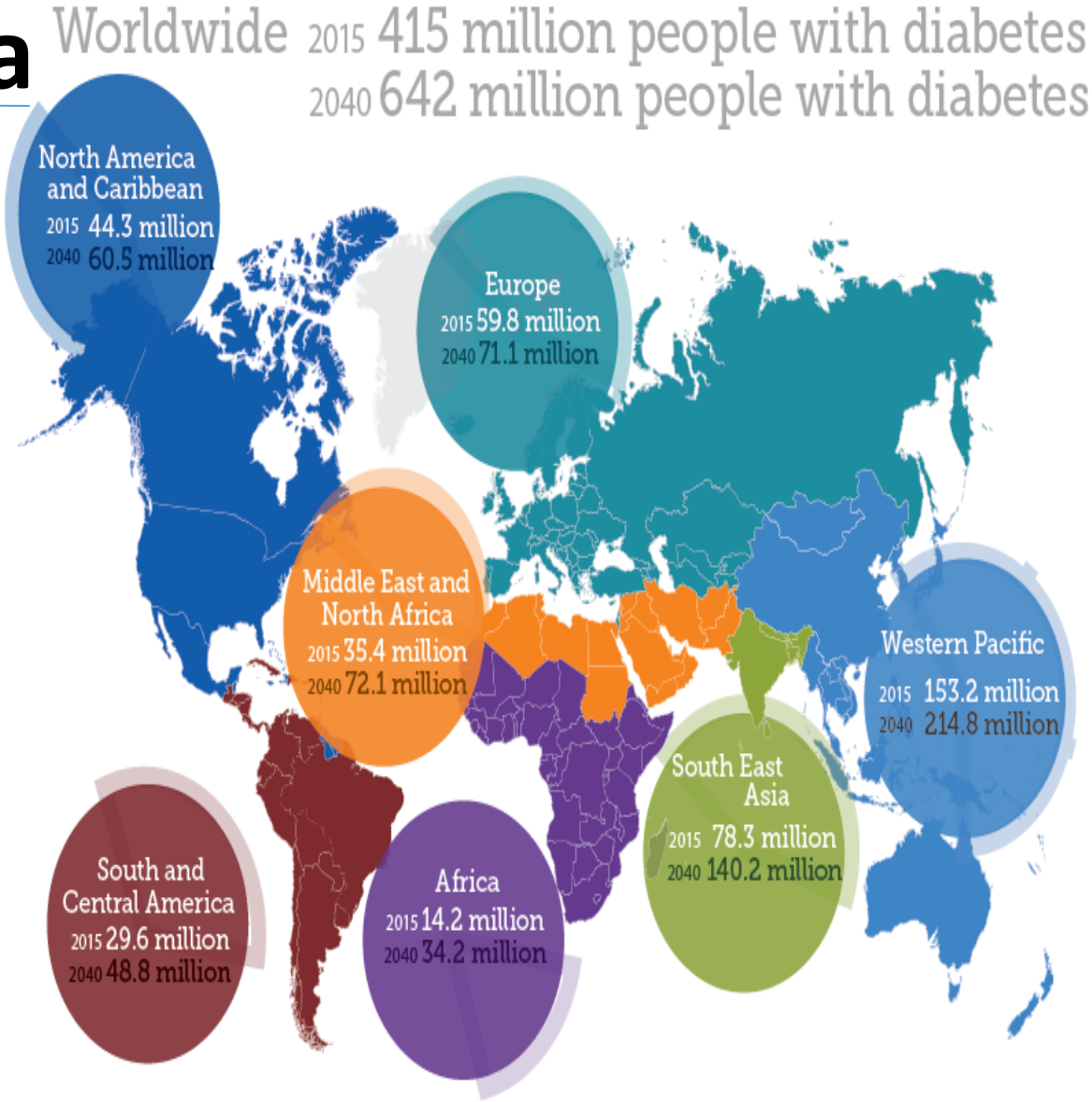
TB-Diabetes burden in India

Prevalence of Diabetes in TB Patients: Recent Studies

Region	TB Patients w/Diabetes	Year Published
Karnataka State, India	32%	2011
Kerala State, India	44%	2012
Tamil Nadu State, India	25%	2012
Texas, USA	39%	2011
Mexico	36%	2011
Tanzania	17%	2011
Pakistan	16%	2012
South Pacific	40-45%	2013

India has the largest number of diabetes mellitus patients (estimated 70 million) and TB-DM

*THE LOOMING CO-EPIDEMIC OF TB-DIABETES: A CALL TO ACTION



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"India lives in 5 centuries at the same time"

Rapid transition from one of the poorest to now 7th largest economy in the world. However ranks 135th among 187 countries on The Human Development Index (a composite measure of health, education, and living standards)

RePORT India Consortium

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What is RePORT India Consortium?

- **Bilateral, multi-organizational collaborative initiative sponsored by the US and Indian Governments under the auspices of INDO-US Vaccine Action Program (VAP) to address the threat of TB in India and across the globe**
  - **US**: The National Institute of Allergy and Infectious Diseases **(NIAID/NIH)**
  - **India**: The Government of India's Department of Biotechnology **(DBT)** and the Indian Council of Medical Research **(ICMR)**

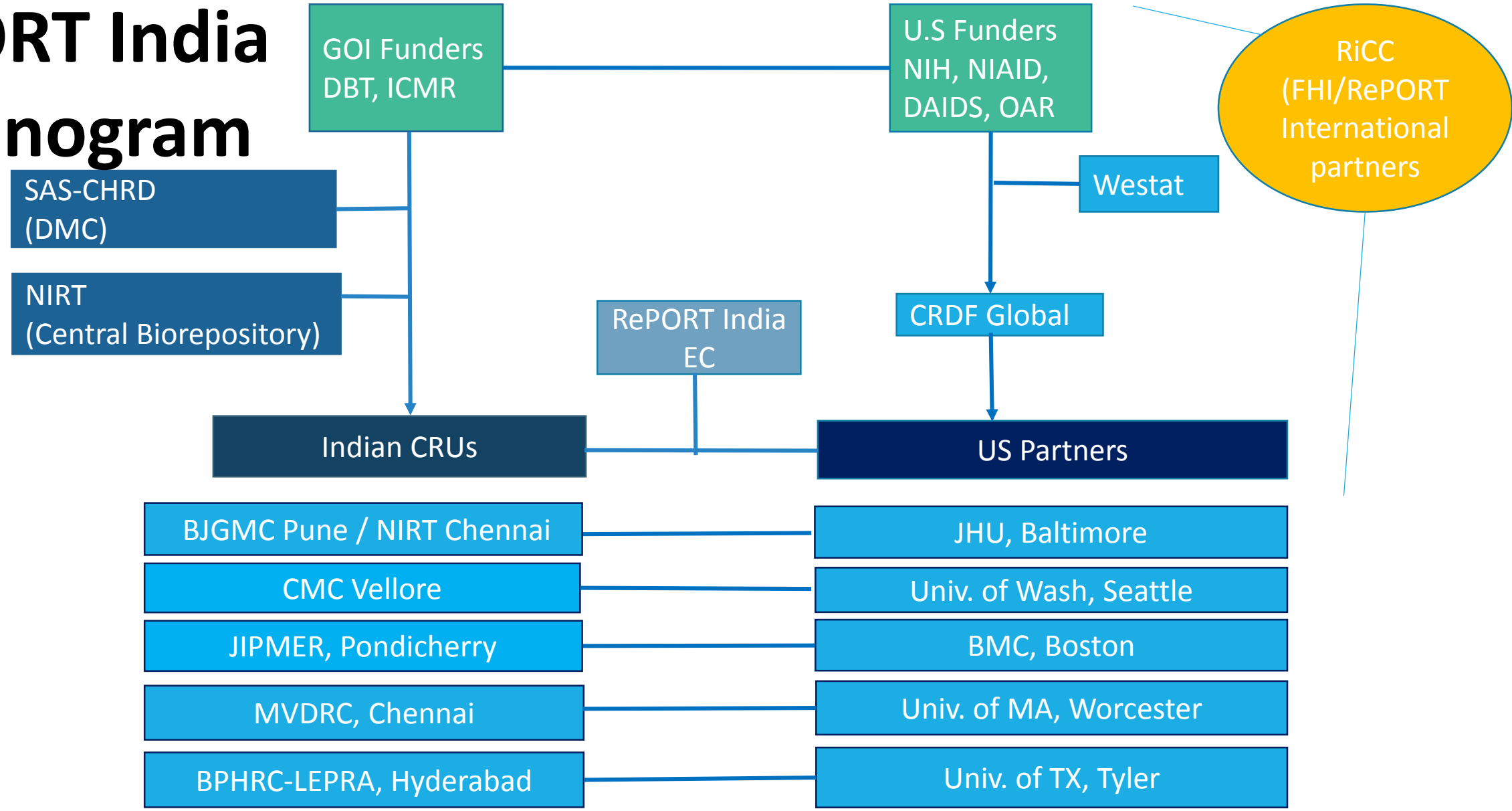
  MISSION:
  - **Advance regional TB science** in India
  - **Strengthen TB research capacity and infrastructure** in India
  - Serve as an entity to **foster research collaboration** within India and internationally, with the aim of carrying out a range of basic and clinical research that can lead to **clinically important biomarkers, vaccines, drugs, and diagnostics**

What is RePORT India Consortium?

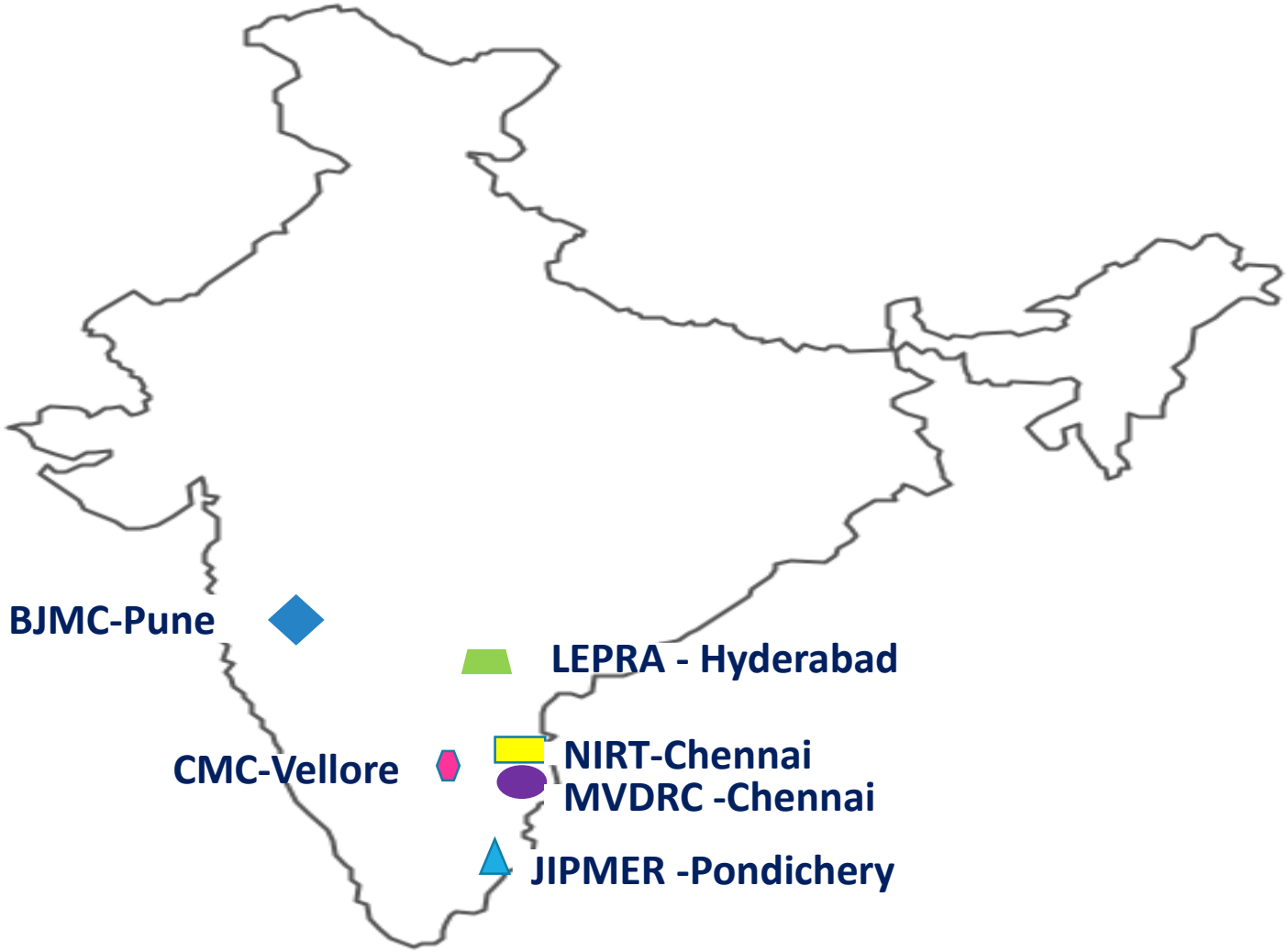
- 5 unique observational TB cohorts in India initiated "Parent Protocols" 2014
- Evaluate TB disease (Cohort A) and TB infection (Cohort B)
- Coordinated by leadership group
  - Composed of PIs, funders, SDMC and Central Repository representatives
- Each cohort linked by "Common Protocol", Central SDMC and Central repository
- Maintain unique research interests while facilitating collaborative research
- Key partnerships

GOAL: To create a resource for the TB research community of a collection of well characterized and standardized samples with accompanying data to investigate critical TB research questions

RePORT India Organogram



RePORT India Site



RePORT India Consortium

Regional Prospective Observational Research for Tuberculosis

IndoUS TB Research Collaboration

Organizational Communications

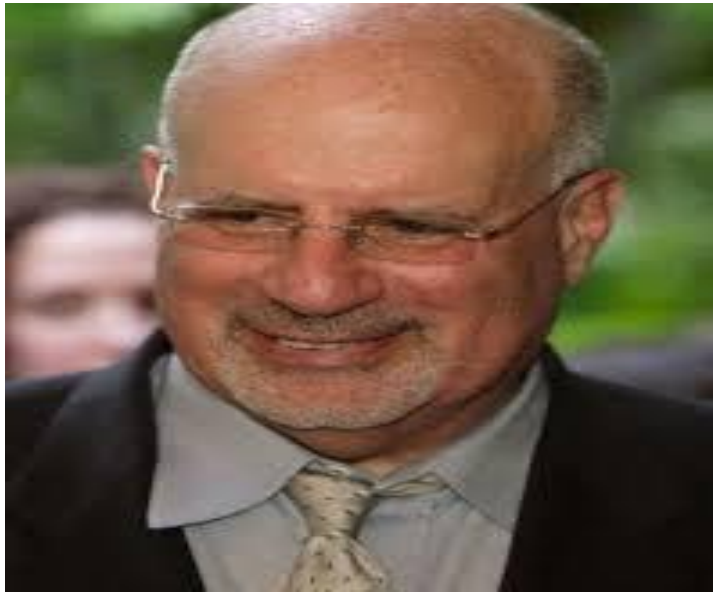
- Coordinate research across cohorts
- Oversee implementation Common Protocol
- Develop and implement scientific agenda
- Establish scientific working groups (Clinical & Basic Science)
- Facilitate sharing of data
- Oversee trans-cohort research projects
- Develop collaborative partnerships with other research programs
- Monthly Executive Committee calls
- Bi-annual in-person meetings

JIPMER & Boston Medical Center

India Co-PI:
Subhash Chandra Parija
Director, JIPMER

India Co-PI:
Gautam Roy
Professor and Head, Dept. of Preventive and Social Medicine, JIPMER

US PI:
Jerrold Ellner
Professor and Chief, Section of Infectious Diseases, BMC
Previously: US RePORT Chair



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JIPMER & Boston Medical Center

Parent Protocol **Biomarkers for Risk of TB and for TB Treatment Failure and Relapse**

Cohort A: PTB n=1,100 **Cohort B HHC n=1500 (≥ 6 years old)**

Objectives

1. Identify biomarkers for risk of treatment failure in the TB case cohort of adults and children ≥ 6 years.
2. Identify biomarkers for risk of development of TB in the household contacts cohort.
3. In both cohorts, determine impact of risk factors (diabetes mellitus, helminth infection, HIV, malnutrition, smoking, alcoholism, and anaemia) on treatment outcome in PTB, development of LTBI and progression from LTBI to disease PTB.
4. Perform network analysis of the transcriptome profiles to define stages in the continuum between LTBI and PTB and their immunologic concomitants.

JIPMER & Boston Medical Center

Abstracts

1. Association between biomass fuel, tobacco use and two-month sputum smear conversion among TB cases in India (*American Thoracic Society Meeting, May 2016*)
2. Association between LTBI and indoor air pollution among household contacts of PTB cases. (*Union Meeting, Dec 2015*)
3. Age and gender distribution of LTBI in a household contact study in India. (*Union Meeting, Dec 2015*)

Grants

1. R01 Impact of Pregnancy on TB, NIH, 2015-18
2. Impact of personal exposure to black carbon on pulmonary TB severity, Potts memorial foundation, 2014-16
3. Role of iron deficiency in resistance of women of child-bearing age to TB, NIH, 2016-17

BJGMC/NIRT & JHU

India PI:
Padmapriyadarsini C
Scientist E, Dept. of Clinical Research, NIRT

Previously
Souyma Swaminathan
now ICMR Director

India co-PI:
Vidya Mave
Clinical Research Director,
BJGMC-JHU Trials Unit

BJGMC-site PI:
Dileep Kadam
Head of Dept of Medicine, BJGMC

US PI:
Amita Gupta
Associate Professor of Medicine,
JHU

BJGMC/NIRT & JHU

CTRIUMPH

Parent Protocol C-TRIUMPH: Cohort for TB research by the Indo-US medical partnership

Cohort A: Active TB: 800 Adult PTB, 200 EPTB, 200 pediatric TB

Cohort B: 1800 HHCs **Cohort C: 150 unexposed controls**

Objectives

1. Measure host and microbial factors associated with TB treatment outcomes in Indian adults and children (Active TB cohort)
   - Residual respiratory impairment following PTB: the lung health sub-study
   - Hair and plasma PK
2. Investigate host and microbial factors associated with progression from infection to active TB disease in adults and children. (Household Contacts)
3. Explore host and microbial factors associated with TB transmission. (HHCs and Control Cohorts)

BJGMC/NIRT & JHU

CTRIUMPH

Publications

Cohort for TB research by the Indo-US medical partnership (c-TRIUMPh): protocol for a multicentric prospective observational study. (*BMJ Open, Feb 2016)*

Presentations

1. Host factors associated with poor respiratory health-related quality of life in PTB (*RePORT International, July 2016)*
2. The association of household air pollution and TB in women and children in Pune (*RePORT International, July 2016)*

Grants

NICHD R01 Impact of immune of changes of HIV and stages of pregnancy on TB

NIAID R21 Hair concentations of anti-TB drugs among HIV-infected and uninfected children in India

Specimen Repository – Cohort A

CTRIUMPH

Type of Specimen	Cohort A (aliquots) BJMC	Cohort A (aliquots) NIRT	TOTAL
PBMC	1592	1467	**3059**
Plasma	8519	4968	**13487**
QGIT	12470	2676	**15146**
Whole blood for mRNA (paxgene)	859	619	**1478**
Whole blood for DNA	142	110	**252**
Urine	6916	2200	**9116**
Hair	748	1	**750**
Stored sputum	1222	1278	**2500**

Specimen Repository - Cohort B

Type of Specimen	Cohort B BJMC (aliquots)	Cohort B NIRT (aliquots)	TOTAL
PBMC	965	1733	**2698**
Plasma	4706	5208	**4706**
QGIT	5962	6120	**9914**
Whole blood for mRNA (paxgene)	487	652	**1139**
Whole blood for DNA	274	325	**599**
Urine	3879	2280	**6159**
Hair	498	1	**499**
Stored sputum	600	1698	**2298**

CTRIUMPH

MVDRC & UMASS

India PI:
Vijay Viswanathan
Head and Chief Diabetologist
MVDRC

US PI:
Hardy Kornfeld
Professor of Medicine
Univ. of Mass

MVDRC & UMASS

Parent Protocol: Effects of Diabetes and Prediabetes on TB Severity (EDOTS)

Cohort A: n=300 PTB >= 30 yrs (w/ and w/o DM)

n=60 controls (no DM, no TB)

Objective

Compare quantitative and qualitative differences in peripheral blood gene expression between diabetic and non-diabetic TB patients longitudinally from presentation through TB treatment.

MVDRC & UMASS

Publications

1. Effect of standard TB treatment on naive, memory and regulatory T cell homeostasis in TB-diabetes co-morbidity, (*Immunology, June 2016)*

2. High prevalence and heterogeneity of diabetes in patients with TB in South India: a report from the EDOTS study, (*Chest, June 2016)*

Abstracts

1. TB susceptibility and metabolic comorbidities (*Keystone Symposium, Feb 2016)*
2. Diabetic immunopathy, (*NIAID/NIDDK workshop, May 2016*)

LEPRA & UTHSCT

India PI:
Vijaya Lakshmi Valluri
Leader, Immunology and Molecular Division, LEPRA

US PI:
Krishna Vankayalapati
Professor and Chair, Dept. of Immunology, U of Texas at Tyler

LEPRA & UTHSCT

Parent Protocol **Identify immunologic markers of persons at highest risk of progression of LTBI to TB**

Cohort B: 2000 HHC >= 6 yrs

Objective

Find novel immune biomarkers that identify persons with LTBI at increased risk for progression to active TB.

-Focus on role of macrophages, Tregs and NK cells

LEPRA & UTHSCT

Presentations Identification of potential biomarkers for development of LTBI by longitudinal follow-up of HHCs of TB patients Kamakshi Prudhula Devalraju *(RePoRT International, July 2016)*

Grant

T-regs mediated immune responses in LTBI and HIV positive individuals, U of Texas, 2015, subcontract

CMC & Univ Cambridge-UWash

India PI:
Dr. D.J. Christopher
Professor, Head of Pulmonary Med.
CMC, Vellore

India co-PI

US co-PI

US PI:
Dr. Lalita Ramakrishnan
Professor, Univ. of Cambridge

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CMC & UWash/Cambridge Univ

Parent Protocol **Host determinants in the eicosanoid pathway modulate the inflammatory response, disease outcome, and treatment responsiveness in TB**

Cohort A: Pulmonary TB Cohort n=200

TB Meningitis Cohort n=200

1. Assess Sputum smear and culture conversion by hyper and hypo-inflammatory *LTA4H* and other genotypes associated with high and low TNF responses to Mtb
2. Assess LTA4H genotype correlates, intensity of the inflammatory response at presentation (CSF total leukocyte count, lipoxin A4 and leukotriene B4), and mortality in TBM

Parent Protocol sample time point – Cohort A

Institution/ Time Point	0	2wk	1mo	2mo	3mo	4mo	5mo	6mo	12mo	18mo	24mo
BJGMC NIRT JHU											
JIPMER BMC											
MVDRC UMACS											
PTB CMC|UW CAMBRIDGE											
TBM CMC|UW CAMBRIDGE											

Parent Protocol sample time point – Cohort B

Institution / Time Point	0	3mo	4mo	6mo	8mo	12mo	16mo	18mo	20mo	24mo	TB
LEPRA Univ TX											
JIPMER BMC											
NIRT BJGMC JHU											

Parent Protocol Screened and Enrolled 2014-16

Screened 2014-2016

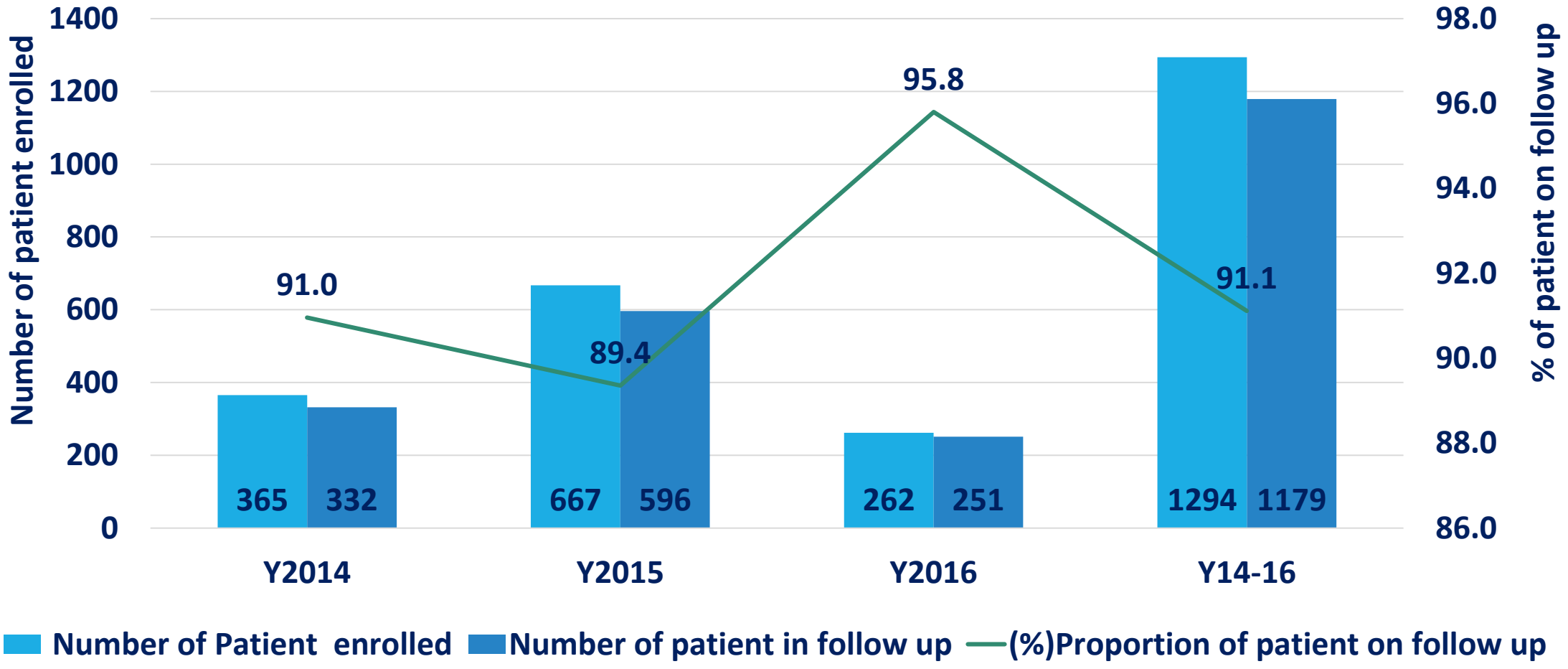
SITE	Cohort A	Cohort B
All Sites	3162	2987

Enrolled 2014-2016

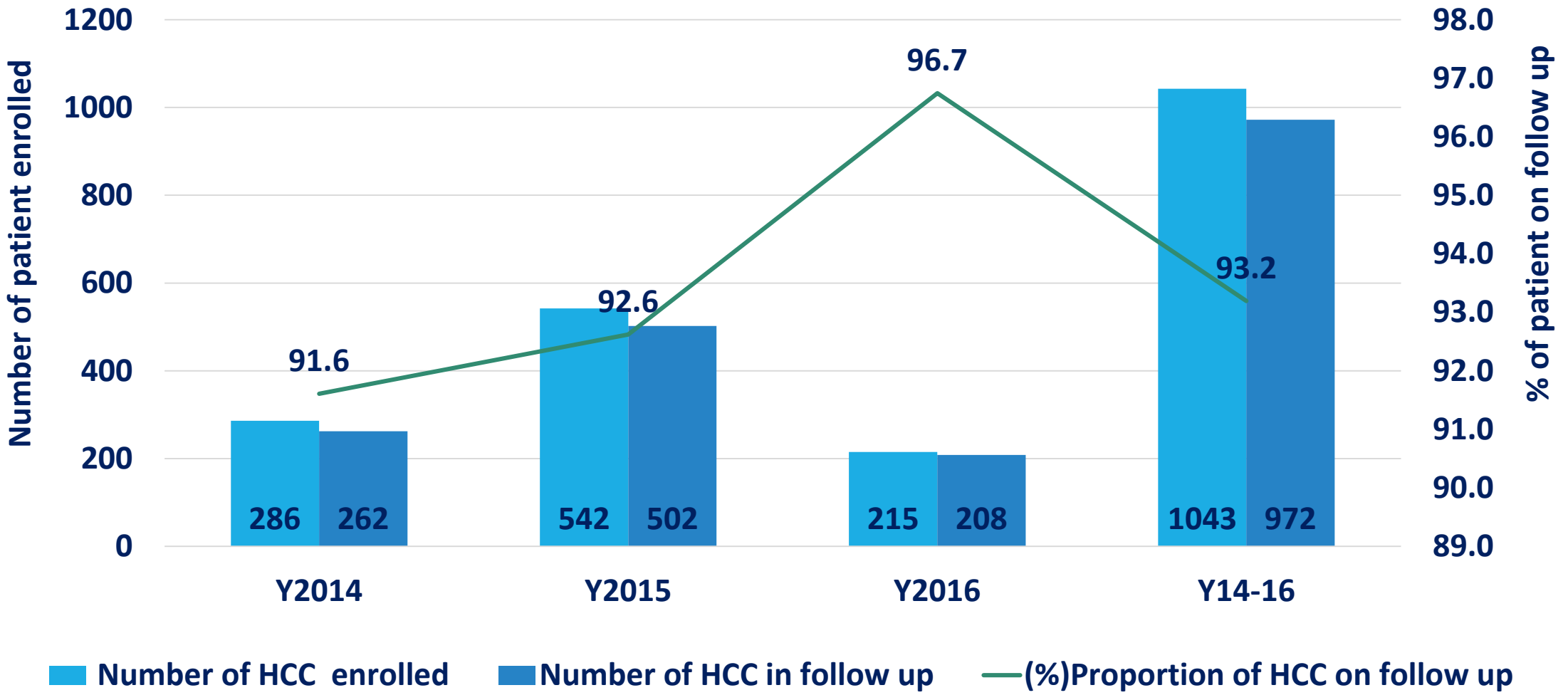
SITE	Cohort A	Cohort B
BJGMC/NIRT	526 (316/210)	745 (335+410)
JIPMER	481	691
MVDRC	251	N/A
LEPRA	N/A	619
CMC	36	84
All Sites	1294	2139

Target actual
Cohort A = 3060
Cohort B = 5500

(%) Proportion of Patient on follow up among the patient enrolled in Cohort A from Year 2014-2016



(%) Proportion of HCC on follow up among the patient enrolled in Cohort B from Year 2014-2016



Parent Protocol Challenges and Lessons Learned : Cohort A

Challenges

- Social problems: stigma of TB, marital issues, and alcoholism
- Refusals due to blood draws
- Dependence of enrollment of household contact
- Lack of family support leading to treatment default

Lessons Learned

- Address sources of TB stigma early
- Build rapport early, including on phone before initial contact
- Locate private setting for visits and reassure participant confidentiality
- Ensure support of family to increase study retention and treatment

Challenges and Lessons Learned : Cohort B

Challenges

- All household members not available during visits
- Unanticipated migrations during study follow-up
- Storage space in freezers

Lessons Learned

- Connect with household contacts during non-working hours and early in the study when visit home
- Continue phone follow-up after TB treatment for better follow-up
- Provide timely abnormal results so can intervene early

Common Protocol

- Minimum set of data and specimens to be collected across all cohorts
- Establish harmonized standards, definitions, and processes for data and specimen collection
- Managed by leadership group and serviced by central DMC and repository
- Enable cross cohort analyses and lab based research projects
- Facilitate collaborations with other research programs

Schedule of Events: Cohort A

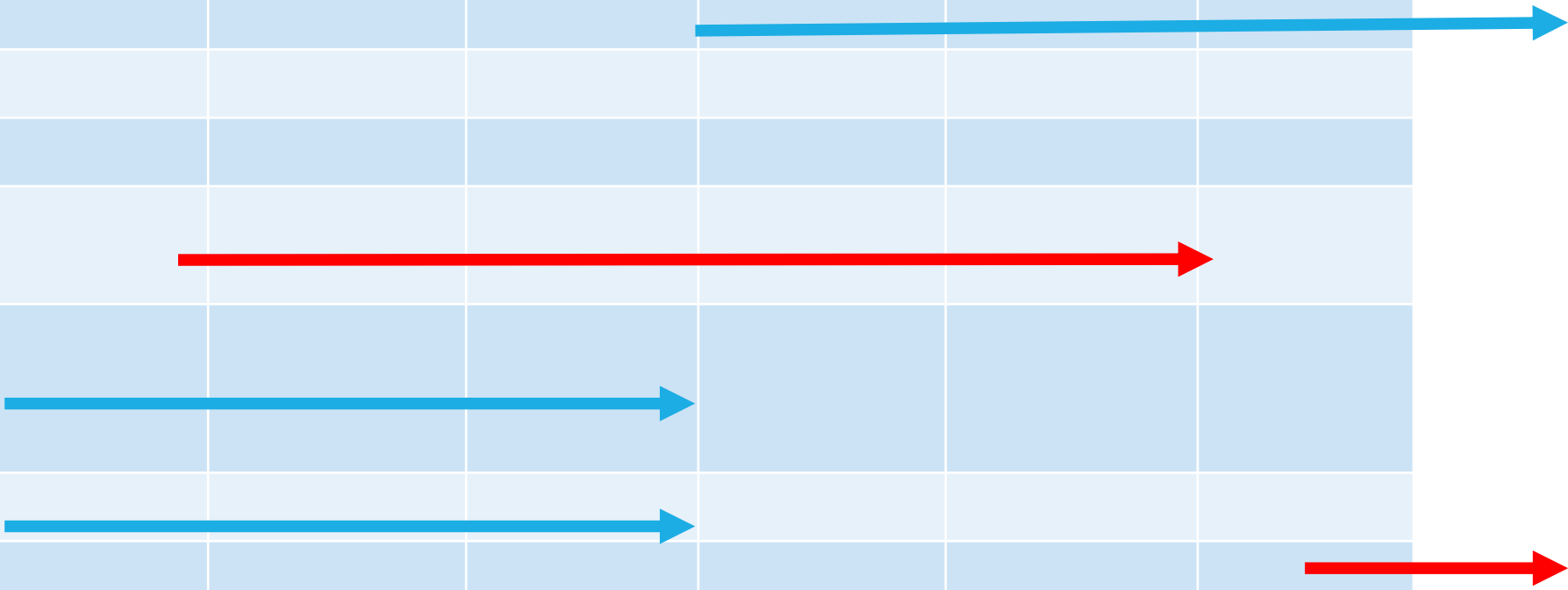
Activities / Visit	SCREENING	BASELINE	Visit 1	Visit 2	END OF TX	6-M POST-TX	TX F/R/W
			DS TB/MDR TB (6-9 mo TX): Week 4 (-1 wk/+3-wks) MDR TB (>18 mo TX)/XDR TB: Week 12 (+4 wks)	DS TB/MDR TB (6-9 mo TX): Week 4 (-1 wk/+3-wks) MDR TB (>18 mo TX)/XDR TB: Week 12 (+4 wks)	(-4 wks/+6 wks)	(-4 wks /+6 wks)[f]	
Informed consent	X						
Eligibility assessment	X	X					
Demographic, medical history, and clinical data		X					
Participant status			X	X	X	X	X
CXR[a]		X		X[a]	X[a]		X[a]
HIV test[b]		X					X[f]
CD4 count if HIV-infected[b]		X					X[f]
CBC and lymphocyte count		X					
HbA1c		X					
Sputum smear & culture[c, d]		X	X	X	X		X
Sputum DST[c, d]		X					X
Mtb isolate subculture for storage		X					X
Whole blood (PAXgene) for storage		X[e]	X	X	X		X
Whole blood (PBMC) for storage		X[e]	X	X	X		X
Plasma for storage		X[e]	X	X	X		X
Whole blood for storage (genetic analyses)		X[e]		X	X		X
Saliva for storage[g] (genetic analyses)		X			X		X
Urine for storage		X	X	X	X		X
Sputum for storage[d]		X	X	X			X

Schedule of Events: Cohort B

Activities / Visit	SCREENING	BASELINE	MONTH 4-6	MONTH 12 (MONTHS 10-14)	MONTH 24 (MONTHS 22-26) and PREM DC	TB ACTIVATION EVALUATION
Informed consent	x					
Eligibility assessment	x	x				
Demographic, medical history, and clinical data		x				
IGRA or TST for eligibility	x					
Participant status			x[e]	x[e]	x[e]	x
Smear and culture from TB activation site[a]						x
Mtb isolate subculture for storage						x
Sputum DST[a]						x
Sputum for storage						x
Whole blood (PAXgene) for storage		x[i]				x
Whole blood (PBMC) for storage		x[i]				x
Whole blood (IGRA) for storage		x[i]				x
Whole blood for storage (genetic analyses)		x[i]				x
Saliva for storage (genetic analyses)[g]		x				x
Plasma for storage		x				x
Urine for storage		x				x
CXR[b]						x
HIV test if status is unknown[c, f]						x
CD4 count if HIV-infected[d, f]						x
CBC and lymphocyte count[f, h]						x
HbA1c[f, h]						x

Common Protocol Timeline 2016

TASK	JUN	JUL	AUG	SEPT	OCT	NOV	DEC
CP Budget Released	X						
v1.0 CP Registration							
v1.0 CP Start							
CRFs							
Database							
v2.0 CP final and IRB approved							
Central Biorepository Set Up (Freezers, etc)							
Training							
v2.0 CP Start							



Central Biorepository for Common Protocol at NIRT

RePORT India Challenges

- Funding $$$
- New consortia growing pains
- Coordination with Common Protocol initiation and other planned studies

Planned Future Studies

- Expansion into MDR/XDR cohorts
  - PREEMPT- RO1 with RePORT India/Brazil sites being resubmitted (Horsburgh/Sterling)
  - Addition of Hinduja site in Mumbai
- Focus on diabetes (Clinical epi, Biomarkers, Immunopath)
- TST and Quantiferon PLUS Comparison Studies (DJ Christopher/Andrea Deluca)
- TB Vaccine trial with VPM Serum Institute

RePORT TST Comparison Summary

Protocol	RePORT TST Comparison Study
Study Objectives:	Compare the performance of latent TB diagnostics (PPD and IGRA among populations of interest, including children and immunocompromised adults
Study Design:	2 PPDs placed at enrollment; SPAN diagnostics (manufactured in India, 5 TU), and Tubersol 5 TU. The mean induration size will be compared. 5 mL of blood drawn and tested for latent TB using the 3rd generation QFT, and 4th generation QGT, or QFT-Plus. Results of the QFT tests will be compared, and related to PPD results. Cross-sectional study with no follow up, though longitudinal data may be abstracted if participants are retained in the RePORT parent protocols
Study Population:	1700 individuals
Study Sites:	Byramjee Jeejeebhoy Medical College and Sassoon General Hospital (Pune, India), the National Institute for Research for Tuberculosis (Chennai, India) Christian Medical College (Vellore, India), Jawaharlal Institute of Postgraduate Medical Education and Research (Pondicherry, India), and LEPRA Society (BPHRC) and Bhagawan Mahavir Hospital and Research Center (BMHRC) (Hyderabad, India)
Study Duration:	18 months
Timeline	BJMC, JIPMER, and CMC Vellore have IRB approval. PPD blinding in process; study to start Sept 2016

RePORT India and TB vaccines

RePoRT India consortium collaborates with Serum Institute of India Pvt Ltd and Vakzine Projekt Management GmbH (VPM) for the Phase III prevention of TB recurrence trial using a novel recombinant BCG vaccine VPM1002

VPM1002-IN-3.01TBR Project Team

Design:	**A multicenter phase III study to evaluate the efficacy and safety of VPM1002 in the prevention of Tuberculosis (TB) Recurrence in pulmonary TB patients after successful TB treatment in India**
Sponsor:	**Serum Institute of India Pvt. Ltd. (SIIPL)**
Clinical Sites:	20 sites spread out all across India (includes 6 RePORT India sites)
Immunology lab:	NIRT Chennai
	Prof. G. Walzl, Stellenbosch University (SUN-IRG)
	Prof. Kaufmann, MPIIB Berlin
CRO:	Parexel / Emmes
Scientific Experts:	Vakzine Projekt Management GmbH
	RePORT consortium (protocol development, immunology, sites)
IMP Manufacturer:	SIIPL

Serum Institute of India Pvt. Ltd.

- Founded in 1966 by a true visionary Dr. Cyrus Poonawalla
- India's # 1 Biotech Company and World's Largest Vaccine Producer (in Volumes) with installed capacity of over 1.4 billion doses of different vaccines.
- Global supplier : 140 countries. (65% of children immunized worldwide get at least one vaccine produced by SIIPL)
- Partner to international agencies such as WHO, PATH, UNICEF, GAVI, PAHO, NIH, NVI/RIVM, CBER/USFDA & BMGF

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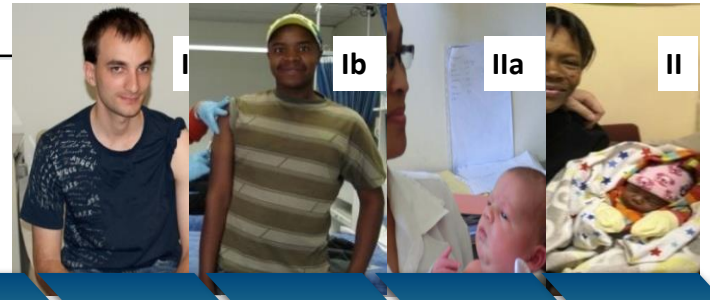
Translational Product Development for VPM1002

< 4 years to bridge the gap from lab to clinics



MAX-PLANCK-INSTITUT FÜR INFEKTIONSBIOLOGIE

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

In-Licensing | GMP-Material | First in Man (ph Ia) | ph Ib | ph IIa | ph II | ph III/IV

VPM1002
as TB **prime** vaccine

2016-2019

VPM1002
as TB **post-exposure** vaccine

phase III

2015-2018

phase I/II NMIBC

VPM1002BC
Immunotherapeutic (non-muscle invasive bladder cancer)

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Product Profile VPM1002

- Parental Strain: BCG subtype Prague
- Genetic Modification: Listeriolysin gene inserted into the bacterial genome (Urease C gene)
- Classification of Biosafety Level: S1 / P1 (**lowest safety level**)

- Post-exposure vaccination with VPM1002 of mice with LTBI delays recurrent TB. Kaufmann et al Max Planck Institute for Infection Biology, Berlin (Gengenbacher et.al.,Microbes Infect. 2016)

VPM1002 Overview completed and ongoing Clinical Development

Development as TB prime vaccine:

✓**Phase Ia:** Evaluation of safety, local and systemic tolerability and immunogenicity of VPM1002 in healthy adult Caucasians compared to reference control (BCG) – **completed with no safety concerns**

✓**Phase Ib:** Evaluation of safety, local and systemic tolerability and immunogenicity of VPM1002 in healthy adult Africans compared to reference control (BCG) – **completed with no safety concerns**

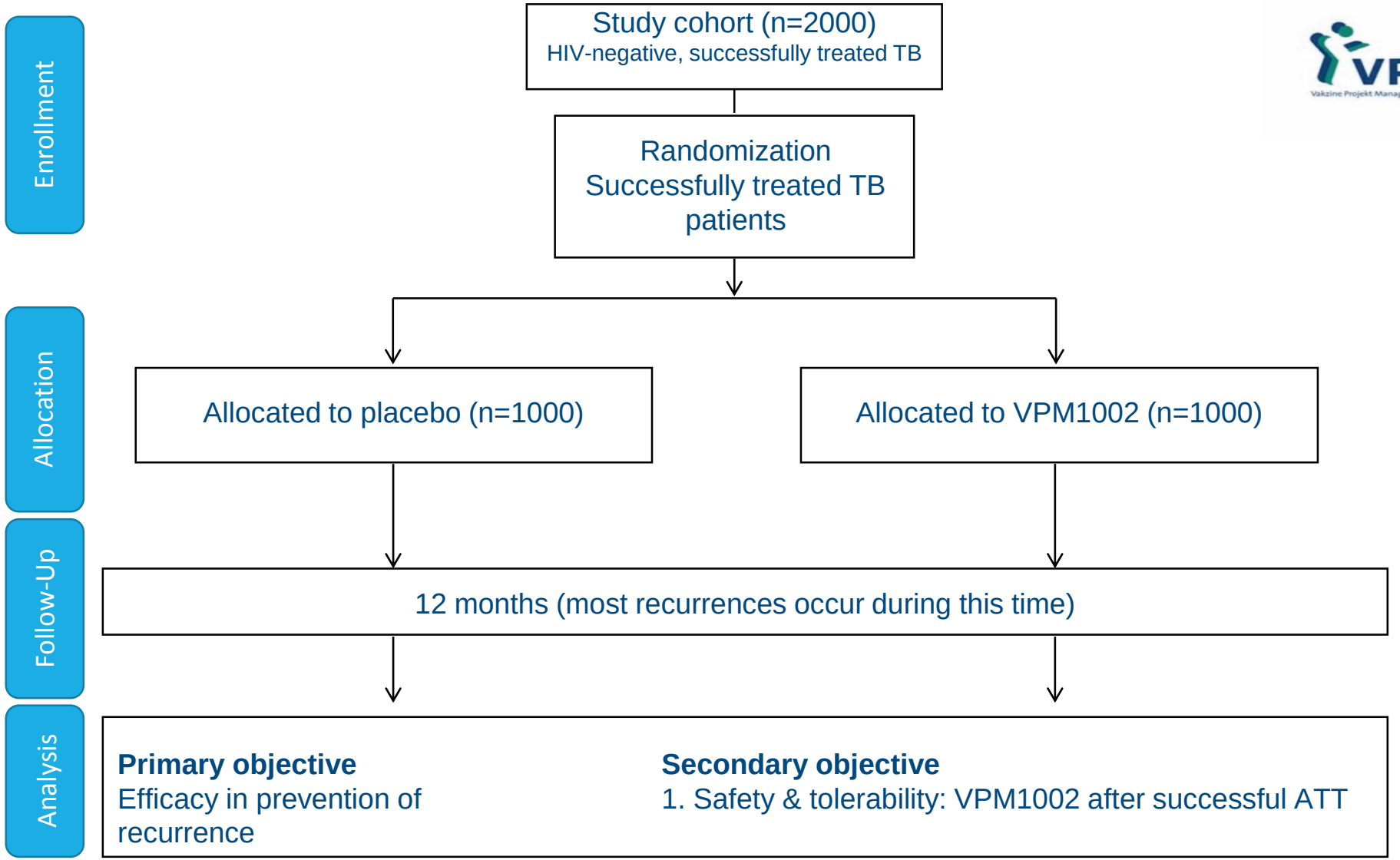
✓**Phase IIa:** Evaluation of safety and immunogenicity of VPM1002 in comparison with BCG in HIV-unexposed, BCG naive newborn infants in South Africa – **completed with no safety concerns**

○**Phase II:** Phase II double-blinded, randomized, controlled study to evaluate safety and immunogenicity of VPM1002 in comparison with BCG in HIV-exposed and HIV-unexposed, BCG-naive newborn infants – **currently ongoing in South Africa (ca. 280 of total 416 infants enrolled)**

Development as Bladder cancer immunotherapy:

○**Phase I:** A Phase I/II Open Label Clinical Trial Assessing Safety and Efficacy of Intravesical Instillation of the Recombinant BCG VPM1002BC in Patients with Recurrent Non-Muscle Invasive Bladder Cancer after Standard BCG Therapy – **currently ongoing in Switzerland (enrollment completed)**

VPM1002 Phase III Prevention of TB recurrence trial



VPM1002-IN-3.01TBR
Objectives and Endpoints I

Primary Objective:

To evaluate the efficacy of VPM1002 in prevention of TB recurrence in pulmonary TB patients who have successfully completed ATT and were declared cured in comparison to placebo.

- **Primary Endpoint:** Bacteriologically confirmed recurrence cases

Secondary Objective:

To evaluate the safety of VPM1002 in TB patients who have successfully completed ATT and were declared as cured.

- **Secondary Endpoints:**
  - Overall recurrence (bacteriologically confirmed or clinically diagnosed)
  - Safety (Solicited local and systemic adverse events within 7 days following study vaccination, unsolicited adverse events, SAEs throughout the study period, all-cause mortality)

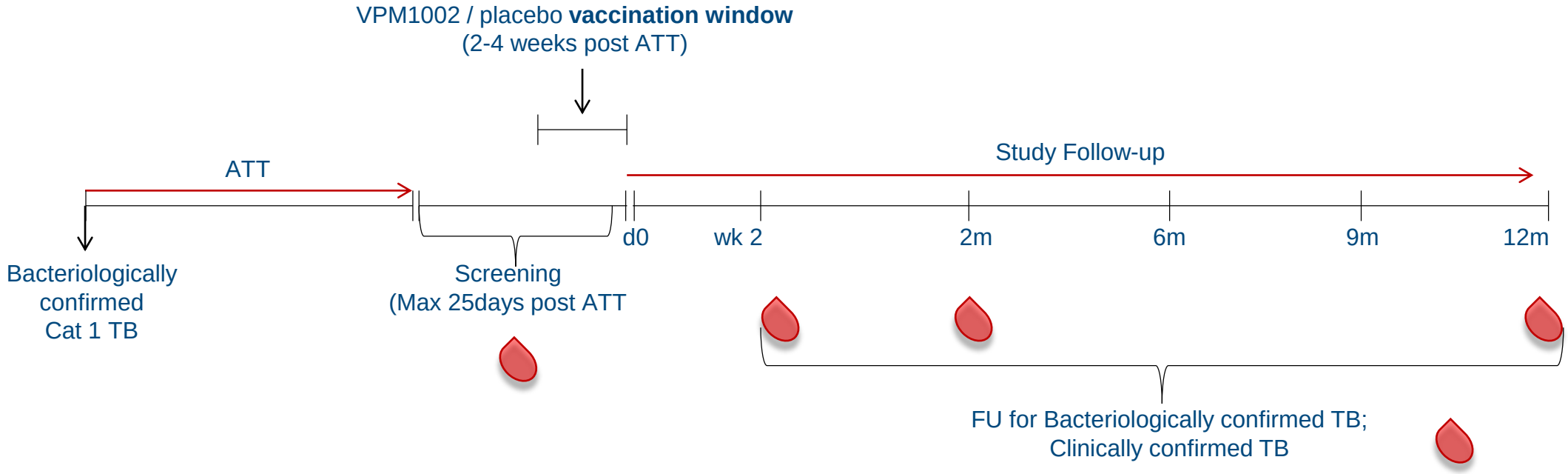
VPM1002-IN-3.01TBR
Objectives and Endpoints II

Exploratory Objective:

- **To assess immunology and transcriptomics as potential correlates of protection and/or Biomarkers in a subgroup of participants.**
- To perform microbiological evaluation of recurrence in a subgroup of recurrent TB patients (i.e. re-infection vs. relapse).
- **To compare immunological difference between VPM1002 and placebo groups.**
- **To compare immunological difference between diabetic and non-diabetic participants.**
- To assess and compare TB mortality

- **Exploratory Endpoint:**
  - Comparison of immunological and transcriptional markers in a subgroup of protected patients and recurrence patients.
  - Comparison of mycobacterial strains within a subgroup of recurrent TB patients between relapse and primary infection.
  - Comparison of immunological difference between VPM1002 and placebo groups.
  - Comparison of immunological difference between diabetic and non-diabetic patients.
  - TB mortality

VPM1002-IN-3.01TBR
Planned study design



BCG vs. VPM1002 Features & Benefits

	Features /Benefits	BCG	VPM1002
Efficacy	Protection against Lab strains (H37Rv)	++	+++
	Protection against clinical TB strains (Beijing)	**-**	**+++**
	Amelioration of TB recurrence in mice	**+**	**+++**
Immunogenicity	Induction of autophagy	+	+++
	Induction of Cross-presentation	+	+++
	Induction of T_H1 immune response	++	+++
	Induction of T_H17 immune response	+	+++
	Induction of multifunctional T-cells	+	++
	Induction of CD8+ T-cells	+	++
	Antigen similarity to *Mycobacterium tuberculosis*	+++	+++
	Induction of cell apoptosis	+	+++
Safety	Persistence	**Long**	**Short**
	Survival of SCID mice	**Death**	**Survival**
	Survival of Interferon γ Knock-out mice	**Survival**	**Survival**
	Abscess formation in vaccinated infants	**Pronounced**	**Less Pronounced**

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INSPIRED BY PEOPLE | DRIVEN BY SCIENCE

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RePORT India Consortium

Regional Prospective Observational Research for Tuberculosis
IndoUS TB Research Collaboration

Thank you