



# Research and Development of new TB vaccines



Foundation to facilitate European efforts  
towards the global development of new  
TB vaccines

[www.tbvi.eu](http://www.tbvi.eu)

# TB burden in 2009

- 14 million prevalent cases of TB
- 9.4 million new cases
- 1.3 million HIV negative deaths, 0.4 million HIV positive; 12 000 deaths in EU (2008)
- 400,000 MDR, 50,000 XDR cases
- 1.9 billion infected with TB (1/3 of world population)

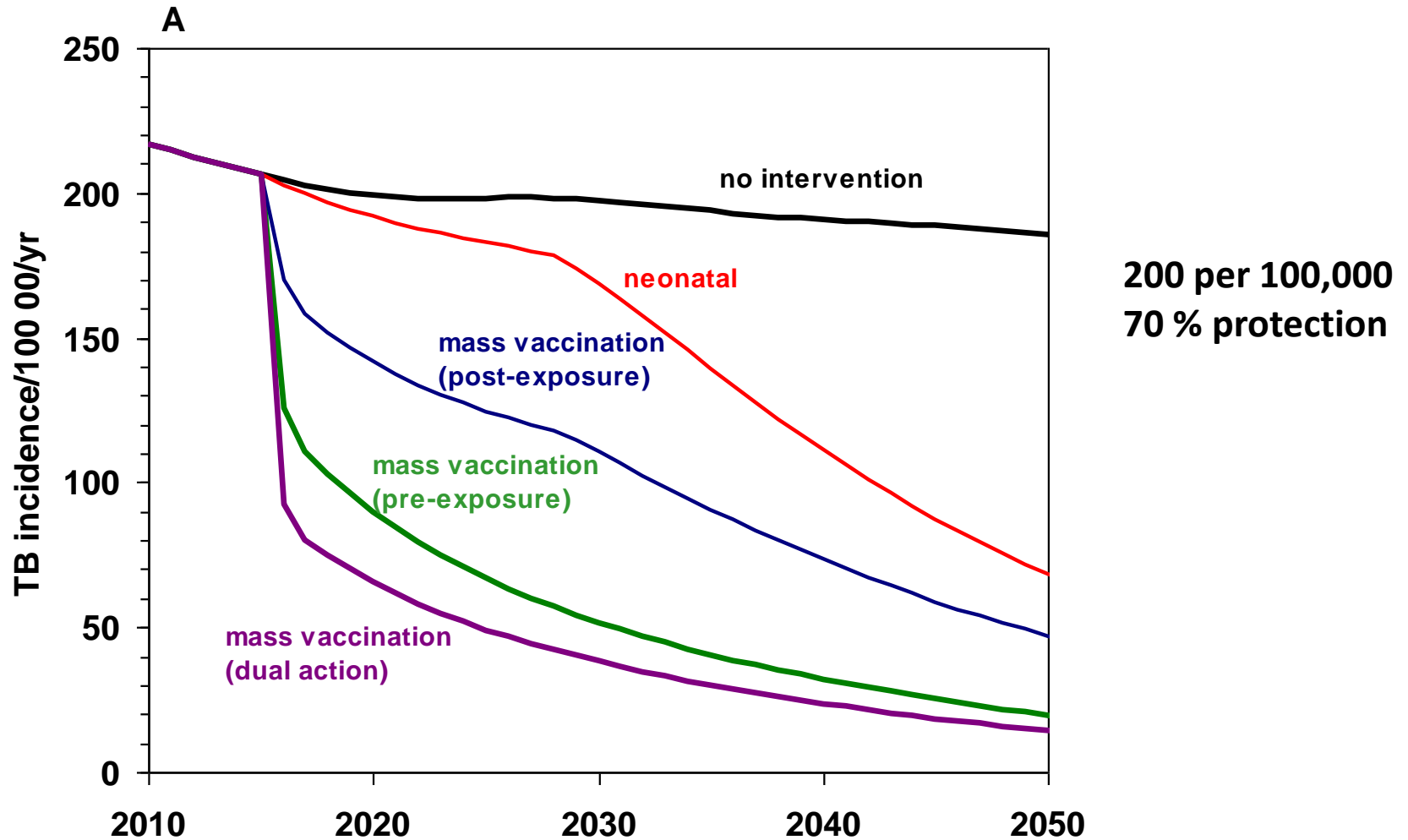


# Why new TB vaccines

- Calmette & Guérin developed the only available TB vaccine: BCG (1906-1921)
- BCG reduces risk of severe pediatric TB disease
- Protection against adult pulmonary TB, which accounts for most TB worldwide, is poor or variable at best
- Not known to protect against latent infection or prevent reactivation
- High risk of disseminated BCG in HIV positive infants



# Predicted impact of new TB vaccine

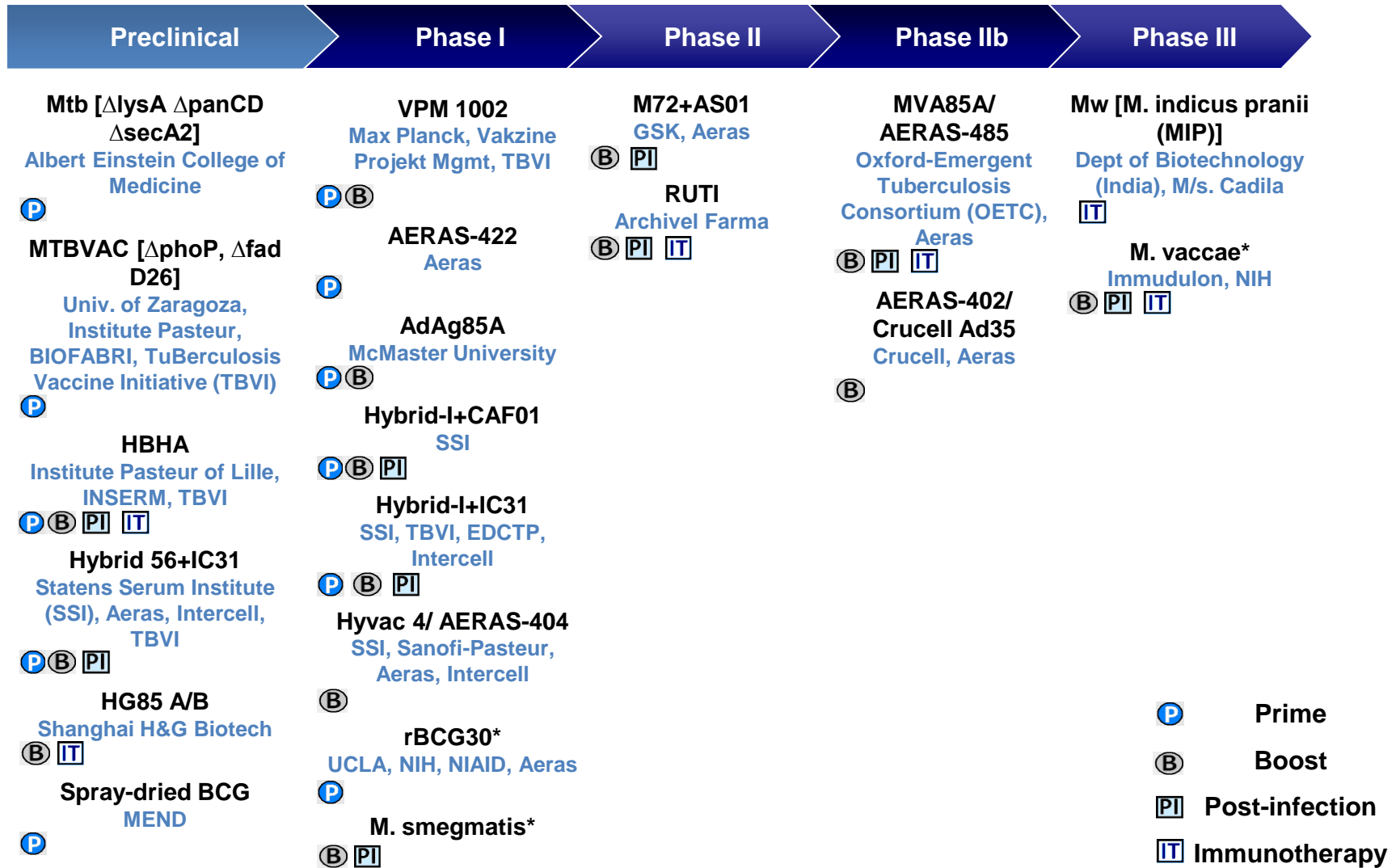


*Young and Dye. 2006. Cell 124:683-7*



# Global TB Vaccine Pipeline

As of December 2010



Preclinical vaccine candidates are not yet in clinical trials, but have been manufactured under Good Manufacturing Practice (GMP) for clinical use and have undergone some preclinical testing that meets regulatory standards.

\* Indicates candidates that have been in clinical trials in the past, but are not currently being tested in clinical trials

# Our History

**2000 – 2004**

Tuberculosis Vaccine Cluster  
EU Framework Programme 5 Integrated Project

**2004 – 2010**

TBVAC  
EU FP 6 Integrated Project

**New sponsors, among others:**

Gates Foundation  
Industry

**2000**

**Present**

**2007**

EU R&D Commission  
Supports creation of a separate entity

**05-03-2008: TBVI Established**



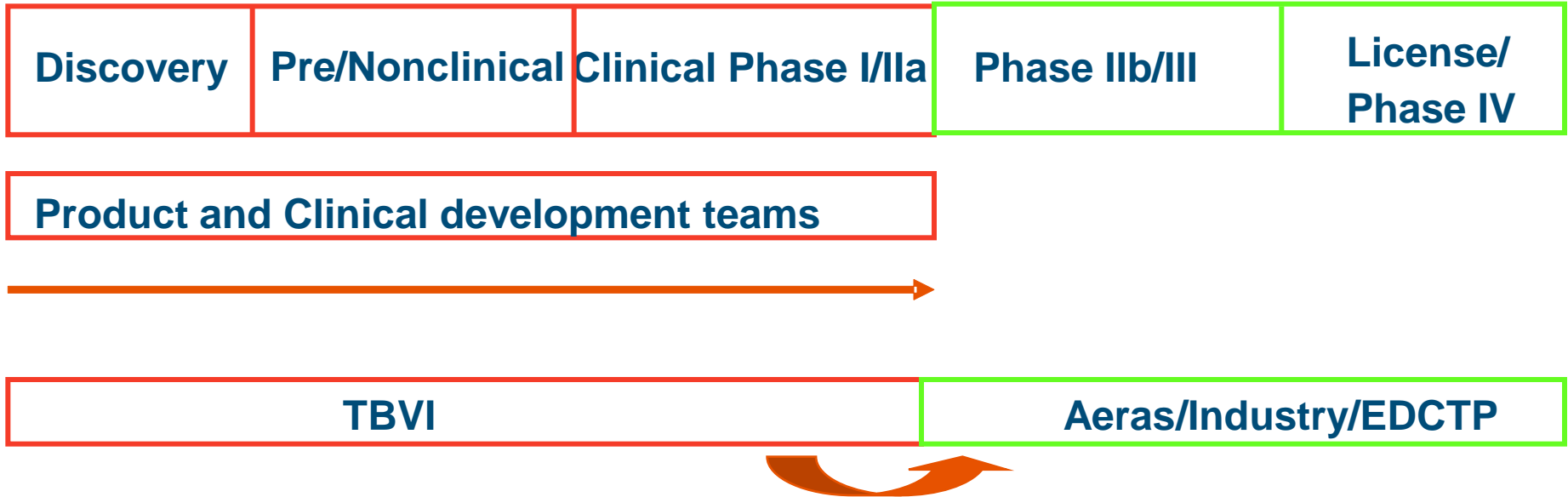
# Our objectives:



- **R&D: *Keep the TB vaccine pipeline filled***
  - Discovery, pre-, nonclinical and clinical development of new vaccines:
    - 8 BCG replacing or boosting vaccines at phase IIa (2009-2018)
  - Develop biomarkers
    - 3 for monitoring and evaluating clinical trial (2015-2018)
  - Building infrastructure
    - 1-3 sites for phase I/II clinical evaluation
- **Advocacy and Resource Mobilization:**
  - > *Grow the global pie for TB R&D (200 mE)*
    - Advocacy for new preventive tools for TB
    - Resource mobilization



# Working model TBVI



Facilitate discovery, preclinical and early clinical TB vaccine development

Responsibility and ownership of candidate vaccine with individual project partners

Guide and advice on development by tailor made product and clinical development teams (PDT/CDT)

Stimulate late clinical development

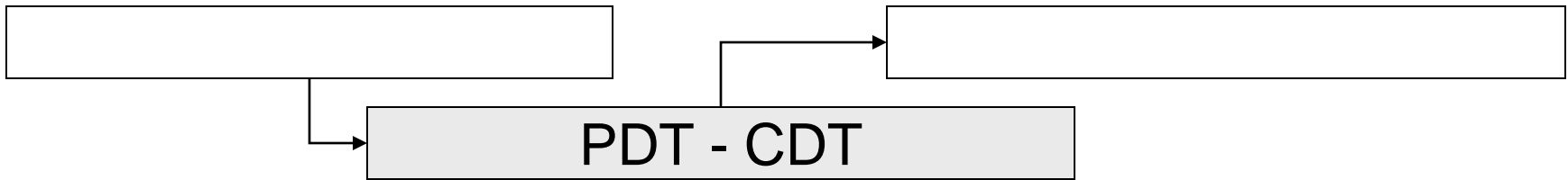




# Fill the gap

Research

Development



Entry criteria:

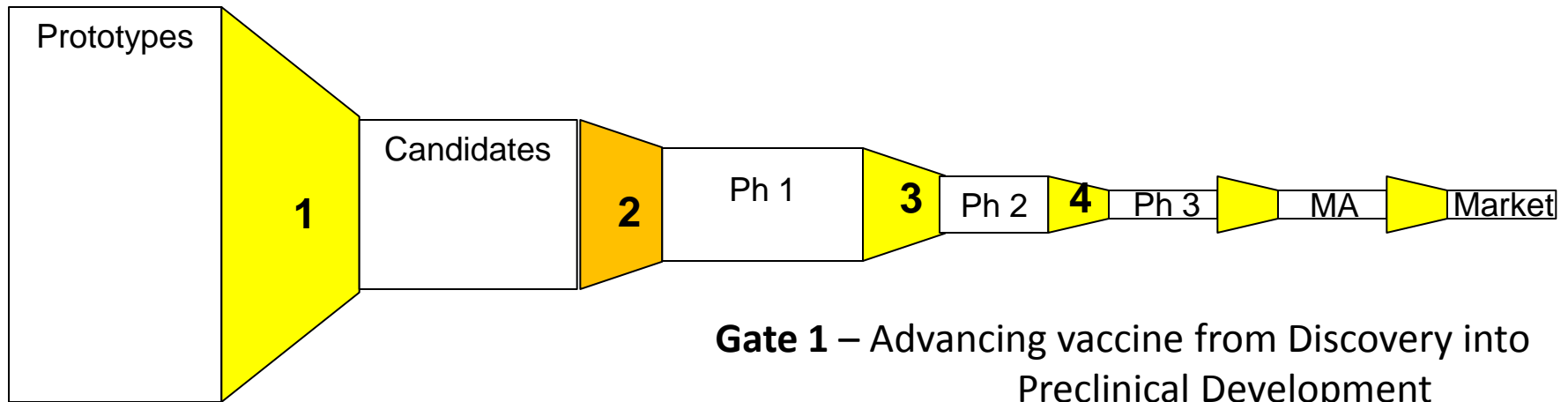
- Select candidate(s)
- Feasibility
- Proof of concept in animals

Go  
Human

- Develop plan and strategy
- Review process & characteristics
- Select manufacturer
- Review animal data; prepare tox & pre-clinical studies; select CRO
- Prepare clinical trial approval form
- Prepare protocol Ph 1; select PI
- Project management & IP



# Stages of development of new vaccines and gates



**Gate 1** – Advancing vaccine from Discovery into Preclinical Development

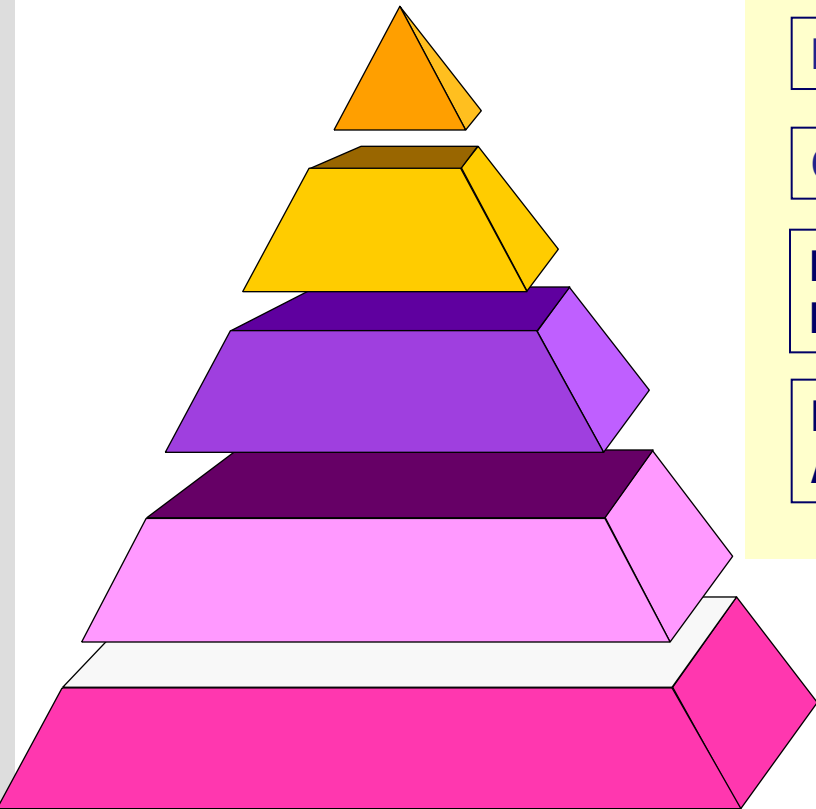
**Gate 2** – Advancing vaccine from Preclinical Development into the Clinic

**Gate 3** – Advancing vaccine from phase 1 to phase 2

**Gate 4** – Advancing vaccine from Phase 2 to phase 3



# TB : Combined vaccination strategies



## Boosting:

New Ags: subdominant, peptidome

Glycolipid Ag: SGL

Latency Ag: Rv2660 (H56), HBHA, Rv3407

Metabolically active antigens:  
Ag85A/B, H1, M72

Adjuvants,  
Antigen  
delivery  
systems

## Priming:

rBCG or rMtb::att

# Vaccine candidates

## Priming

### Phase I

- rBCG::Hly (VPM1002)

### Preclinical to nonclinical

- att. MTB:PhoP (MTBVAC)
- 6 rBCG
- 1 att. Mtb.

### Discovery

- 3 rBCG
- 6 att. Mtb
- 1 att. Mbovis

## Boosting

### Phase I/II

- (MVA/85A)
- 72M/ASO1b
- H1/IC31
- H1/CAF01

### Preclinical to nonclinical

- 4 subunit/adjuvant
- 1 Lipid based
- 2 Viral delivery based

### Discovery

- 1 Subdominant antigens
- 1 Peptidome antigens
- 1 Lipid antigens
- 1 Reactivation antigens
- 1 Resuscitation antigens
- 2 Latency antigens



# NEWTBVAC

- Consortium of 32 European + 3 Asian Partners
- 1-1-2010 - 31-12-2013
- 12 m€ EC
- Sustain and innovate current European vaccine and biomarker pipeline
- Second generation vaccines and/or combination of vaccines that will also impact on reduction of disease in latently infected individuals



# TBTEA:

*Collaboration and integration of Tuberculosis Vaccine Trials in Europe and Africa*

## **Objectives**

To build a sustainable European-African platform:

- where knowledge and know-how on clinical trials of ongoing and future clinical TB vaccine evaluations in Europe and Africa can be exchanged,
- where joint activities can be explored and coordinated,
- where clinical trials capacity will be improved, broadened, integrated, and where overlap and unnecessary duplication of work will be prevented by the creation of synergies.

**The platform will have a specific emphasis on current and novel assays for evaluating the immune response to vaccination in a clinical setting - MVA85A, VPM1002, MTBVAC, HBHA**

**Start:** 1 September 2011 – June 2013



# Our research partners 2011

## Argentina

- INTA Institute of Biotechnology

## Belgium

- Université Libre de Bruxelles
- Scientific Institute of Public Health
- GSK-Biologicals

## Denmark

- Statens Serum Institute

## Ethiopia

- Armauer Hansen Research Institute

## Finland

- FIT Biotech

## France

- Centre National de la Recherche Scientifique
- Institut National de la Santé et de la Recherche Médicale
- Institut Pasteur
- Institut Pasteur de Lille
- Institut Mérieux
- PX' therapeutics

## Germany

- University of Lübeck
- Technical University of Munich
- Max-Planck Institute for Infection Biology
- University of Tübingen
- University of Ulm
- University of Erlangen-Nürnberg
- Vakzine Projekt Management

## Italy

- National Institute for Infectious Diseases "Lazzaro Spallanzani"
- University of Palermo
- Istituto Superiore Di Sanita
- University of Padua

## Netherlands

- Central Veterinary Institute of Wageningen UR
- Biomedical Primate Research Centre
- Leiden University Medical Center
- Free University of Amsterdam
- National Institute for Public Health and the Environment

## Portugal

- University of Porto

## Republic of Korea

- Institut Pasteur Korea
- Educational Foundation Yonsei University
- International Vaccine Institute

## Senegal

- Espoir Pour La Santé (EPLS)

## South Africa

- University of Cape Town
- Stellenbosch University

## Spain

- Universidad de Zaragoza Facultad de Medicina
- Fundacio Institut De Investigado de Ciencies De La Salut Germans Trias I Pujol
- CZ Veterinaria/BIOFABRI

## Switzerland

- Institute for Research in Biomedicine
- University of Geneva
- University Hospital of Basel
- University of Zürich
- Centre Hospitalier Universitaire Vaudois
- Fondazione Per L' Istituto Di Ricerca in Biomedicina

## Uganda

- The Infectious Diseases Institute (IDI) at Makerere University

## United Kingdom

- Health Protection Agency Porton Down
- University of Birmingham
- Aston University
- Manchester University Medical School
- Imperial College of Science Technology and Medicine
- National Institute for Biological Standards
- University of Oxford
- London School of Hygiene and Tropical Medicine
- Veterinary Laboratory Agencies

Our research partners





# Our Allies

- Aeras, Rockville, USA
- European and Developing Countries Clinical Trials Partnership (EDCTP), The Hague, The Netherlands
- European Foundation Centre, Brussels, Belgium
- European Vaccine Initiative (EVI), Heidelberg, Germany
- Fundacion Ramon Areces, Madrid, Spain
- Fondation Mérieux, Lyon, France
- Karolinska Institute, Stockholm, Sweden
- KNCV Tuberculosis Foundation, The Hague, The Netherlands
- Les Amis du Fonds Europe, Paris, France
- Médecins sans Frontrières, Geneva, Switzerland
- PATH Malaria Vaccine Initiative, Bethesda, USA
- Sclavo Vaccines Association, Italy
- Stop TB Partnership, Geneva, Switzerland
- The Brighton Collaboration, Basel, Switzerland
- The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), Geneva, Switzerland
- TB Europe Coalition
- NIH Tuberculosis Research Unit (TBRU), Cleveland, USA
- NIH, Bethesda, USA
- WHO, Geneva, Switzerland



# Our donors/sponsors

- EU 7<sup>th</sup> framework programme
- Bill & Melinda Gates Foundation
- Calouste Gulbenkian Foundation
- FIT Biotech
- Institut Mérieux
- GSK Biologicals
- EDCTP





**TBVI**

TuBerculosis Vaccine Initiative

Thank you for  
your attention!



Foundation to facilitate European efforts towards  
the global development of new TB vaccines

Visit us at [www.tbvi.eu](http://www.tbvi.eu) or [www.twitter.com/tbvi\\_eu](https://www.twitter.com/tbvi_eu)