AERAS

Approaches to TB Vaccine Development

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Aeras Global TB Vaccine Foundation

Beyond BCG: Towards an Effective New Vaccine for TB
All Party Parliamentary Group on Global Tuberculosis
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London

Link between public policy and public health

The tax on light and air leads to an increase in TB

UK Leadership on Global Health and Research

- Key donor to GAVI Alliance, Global Fund to Fight Aids, TB and Malaria and Stop TB Partnership
- Supporting AMC for pneumococcal vaccines
- New research strategy nearly doubles funding for development research by 2010/2011
- Global leader in recognition and support of PDPs for neglected diseases

Accelerating TB Vaccine R&D through Product Development Partnerships (PDPs)

- Non-profit enterprises created to accelerate R&D for new products to fight AIDS, TB, malaria and other neglected diseases
- Manage resources and partnerships from across public, private and philanthropic sectors
- Complements partners expertise, facilities and capacity
- Utilize a portfolio management approach
- Act as a catalyst to advance new products through the development pipeline towards registration and launch
- Range from “virtual” to “bricks and mortar” depending on availability of external capacity
- Commitment to access, availability and affordability

Aeras Global TB Vaccine Foundation

Mission:

To develop new, more effective TB vaccines and ensure their affordability and availability to all who need them.

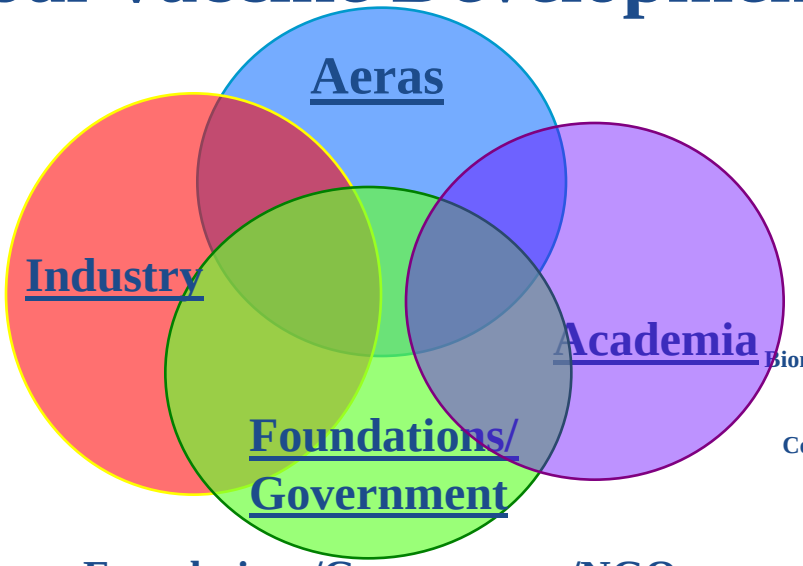
Goals:

- A more effective, safe and affordable TB vaccine
- Identify correlates and surrogate markers of vaccine induced protection
- Develop second generation TB vaccines with increased potency and broader protection

Aeras Global Vaccine Development Partners

Industry

GSK, UK
Crucell, Netherlands
Sanofi/SSI, Denmark
ImmunoBiology, UK
Wuhan Biologicals, China
Serum Institute, India
Thymed, Germany
Alphalyse, Denmark
Japan BCG Laboratory, Japan
Korean Institute of TB, Korea
Cyncron, Denmark
Cellestis, Australia
Immune Solutions, New Zealand
Larimer, U.S.
Sanofi Pasteur, France
Smittskyddsinstitutet, Sweden
BIOCON, U.S.
Emergent BioSolutions, U.S.
Intercell, Austria
Spring Valley Laboratories, U.S.
Statens Serum Institute, Denmark



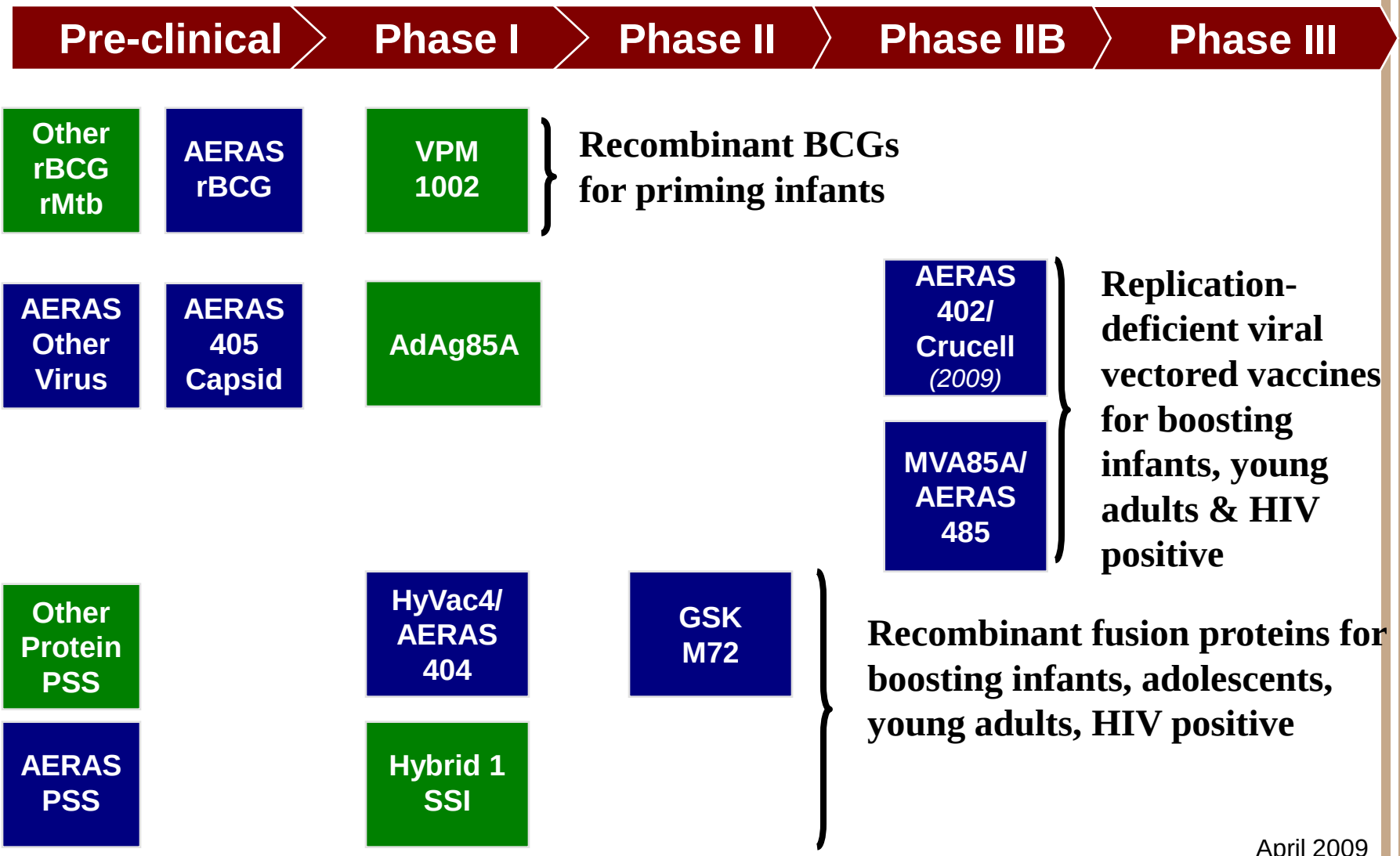
Foundations/Governments/NGOs

Bill & Melinda Gates Foundation, U.S.
Ministry of Foreign Affairs of Denmark
The Netherlands Ministry of Foreign Affairs, The Netherlands
Centers for Disease Control and Prevention (CDC), U.S.
Fogarty International Center and NIAID, National Institutes of Health, U.S.
Research Council of Norway, Norway
Wellcome Trust, UK
AIDS Fondet, Denmark
Cambodian Health Committee, Cambodia
European and Developing Countries Clinical Trials Partnership (EDCTP), European Commission
LHL/ The Norwegian Association of Heart and Lung Patients, Norway
Planeta Salud, Spain
Manhiça Health Research Centre, Mozambique
Medicine in Need (MEND), U.S.
STOP TB Partnership, Switzerland
TB-Alert, UK
TBVI, Europe

Academia

Oxford University, UK
University of Wales, UK
SATVI, South Africa
St. Johns Research Institute, India
Makerere University, Uganda
Kenya Medical Research Institute, Kenya
Karolinska Institute, Sweden
Wuhan University, China
Albert Einstein College of Medicine, U.S.
Arizona State University, U.S.
Biomedical Primate Research Center, The Netherlands
Case Western Reserve University, U.S.
Central Institute for Tuberculosis, Russia
Centre for International Health at the University of Bergen, Norway
Colorado State University, U.S.
Emory University, U.S.
Food and Drug Administration, U.S.
FIND, Switzerland
Harvard University, U.S.
International AIDS Vaccine Initiative (IAVI)
Johns Hopkins University, U.S.
KNCV Tuberculosis Foundation, The Netherlands
Leiden University Medical Center, The Netherlands
Life Science Research Israel (LSRI), Israel
Max Planck Institute for Infection Biology, Germany
McGill University, Canada
National Cancer Institute, The Netherlands
New York University, U.S.
Oregon Health Sciences University, U.S.
Public Health Research Institute
Stanford University, U.S.
Saint Louis University., U.S.
University of Bergen, Norway
University of California-Davis, U.S.
University of California- San Francisco, U.S.
University of Maryland, College Park, U.S.
University of Tampere, Finland
Vanderbilt University., U.S.
Walter Reed Army Institute of Research, U.S.

Current TB Vaccine Pipeline



April 2009

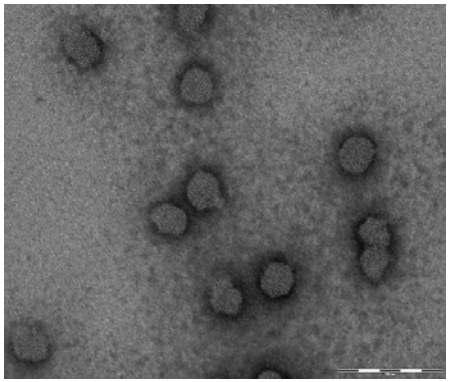
Recombinant BCG (rBCG) – Goals for Making a Better BCG

- Safer
  - Incorporates escape from the endosome where it hides
  - Safer in HIV infected infants or others with immune-suppression
  - May eliminate need for HIV screening of infants prior to rBCG
- More immunogenic
  - BCG or rBCG boosted with another TB vaccine (either viral vector or protein + adjuvant) is much better than either vaccine alone
  - Constructed to over-express antigens from each stage of the TB life cycle
- Prevent infection and reactivation utilizing “prime-boost” regimens
- A new vaccine candidate with all of these properties is expected to enter the clinic in 2009

Developing Novel Technologies: Aerosol Delivery of New TB Vaccines

- Very small particles (2-4 microns) get deep into the lung, where infection occurs
- Two methods of creating and delivering these particles are being developed
  - Nebulizer with laser drilled filter for liquid vaccines
  - Spray drying that yields dry powder particles delivered by a low-cost plastic inhaler
- Preclinical studies with US NIH indicate potential for better immune response than with injections
- Aerosol delivery may provide an easy, affordable delivery mechanism that could eliminate the need for needles and cold chain and provide superior protection

Spray Drying



Purified nucleocapsid

Building Manufacturing Capacity

- Reduce the cost and time to manufacture and deliver vaccines to all who need them
- Produce enough bulk doses of rBCG (~200 million/year) and nucleocapsids (>1 billion/year) to meet the world's estimated need
- Work with partners in emerging economies such as India, China, Brazil and South Africa to produce, fill, finish and distribute vaccines at the lowest possible price
- Ensure uniformity of quality
- Minimize lag time between licensure and distribution

Fermentation Tanks
Aeras Manufacturing Facility
Rockville MD USA

Developing Field Sites for TB Vaccine Research

- Clinical trials are conducted in countries with a high burden of TB
  - New vaccines need to be tested in areas with high enough incidence rates to determine efficacy
  - Trials in endemic countries will demonstrate vaccine safety and efficacy in the populations that most need it
  - Safety trials are conducted in US and/or Europe before initiating trials in high burden countries
- Vaccine trials require community outreach, education and engagement
- Aeras partners with local research institutions to establish field sites and conduct clinical research
  - Scientific expertise combined with knowledge of research environment
  - Build local infrastructure and health care/research capacity
  - Contributes to development of local clinical research profession

Challenges to Site Development

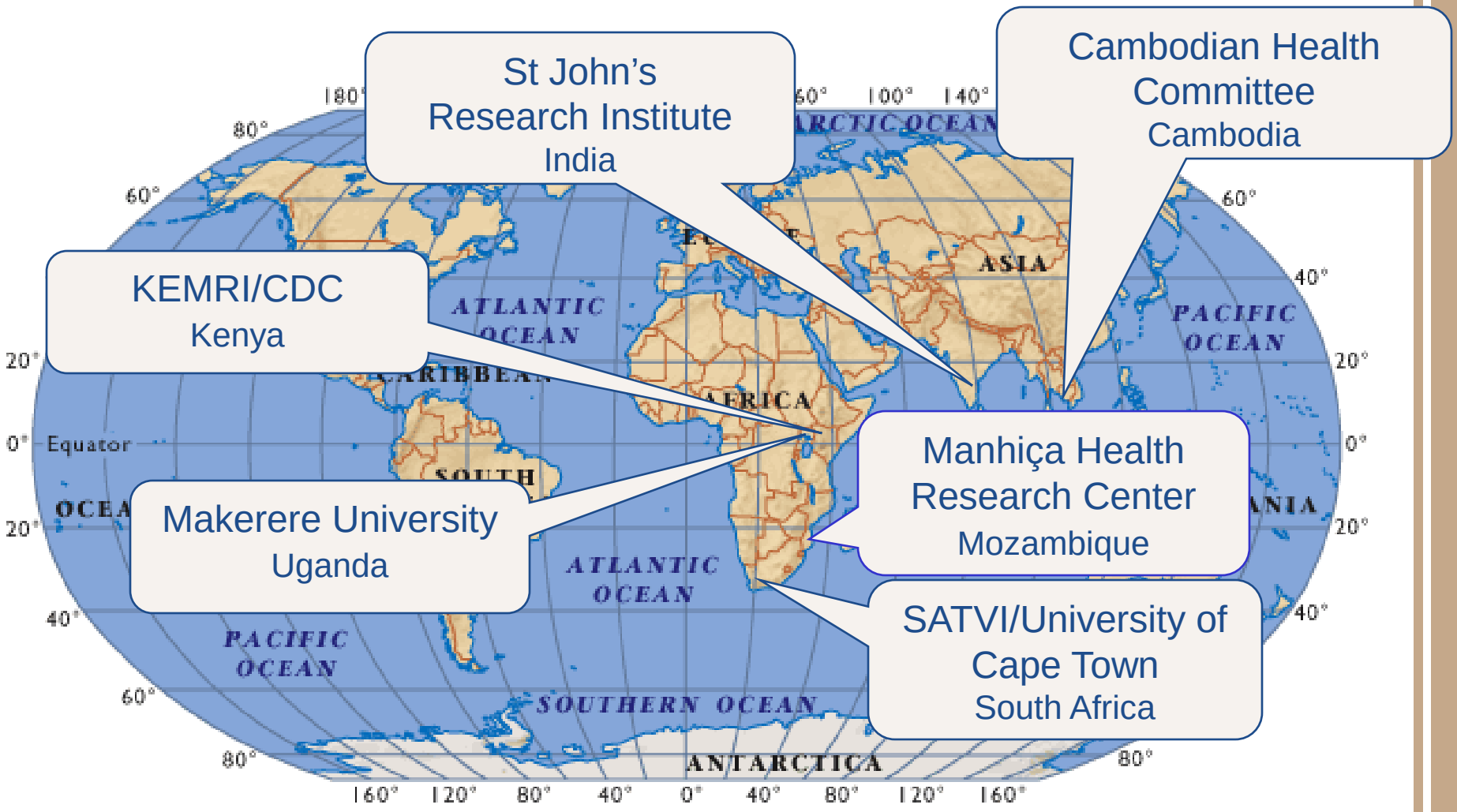
Areas with very high rates of TB

- Usually do not have capacity to maintain Good Clinical Practice (GCP)
- Do not have capacity for TB diagnosis by culture
- Do not have capacity for collection and storage of blood for immunology
- Do not have adequately trained staff at the community level

Palamaner, India site before development

Lab at Palamaner, India site after development

Aeras Partnerships in Clinical Development

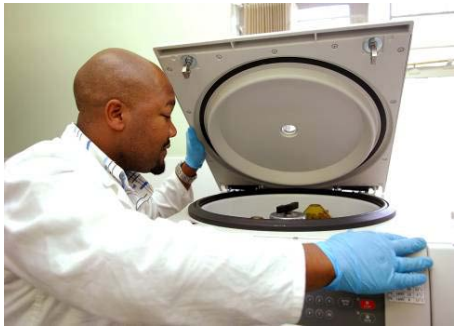


TB Vaccine Site Development Activities

- TB diagnosis laboratory set-up and maintenance
- Epidemiology cohort studies
- Establishment of a Professional Development Program
- Implementation and maintenance of Quality Management Systems
- Data management infrastructure set-up or augmentation
- Clinical trials of vaccine candidates

Example of Site Development: South Africa

- Partnership with South African Tuberculosis Vaccine Initiative (SATVI)
- Field site developed in Worcester (~120 km from Cape Town)
- Infrastructure developed:
  - Approximately $14 million invested over 7 years to build infrastructure
  - State-of-the-art immunology laboratory
  - Highly skilled staff capable of performing the duties necessary to maintain the infrastructure and execute clinical research
  - Clinical and office facilities
  - Professional Development Program (Siyantinga- “Reach for the Stars”) – program initiated in 2001
  - Resource Center established in 2005



Accomplishments in South Africa

- BCG randomized clinical trial from 2001-2006: 11, 680 infants vaccinated and followed-up for two years
- Epidemiology studies involving more than 11,500 participants
- Conducting Phase I and Phase II studies of 4 vaccine candidates, several additional trials planned for 2009
- Initiating Phase IIb trial of a new TB vaccine
- 231 staff trained since 2004, including 162 female staff
- Establishment of a locally maintained Quality Management System
- Establishment of a locally maintained robust data capture mechanism
- Most advanced site for large-scale TB vaccine trials in the world

Capacity Building at Other Partner Sites

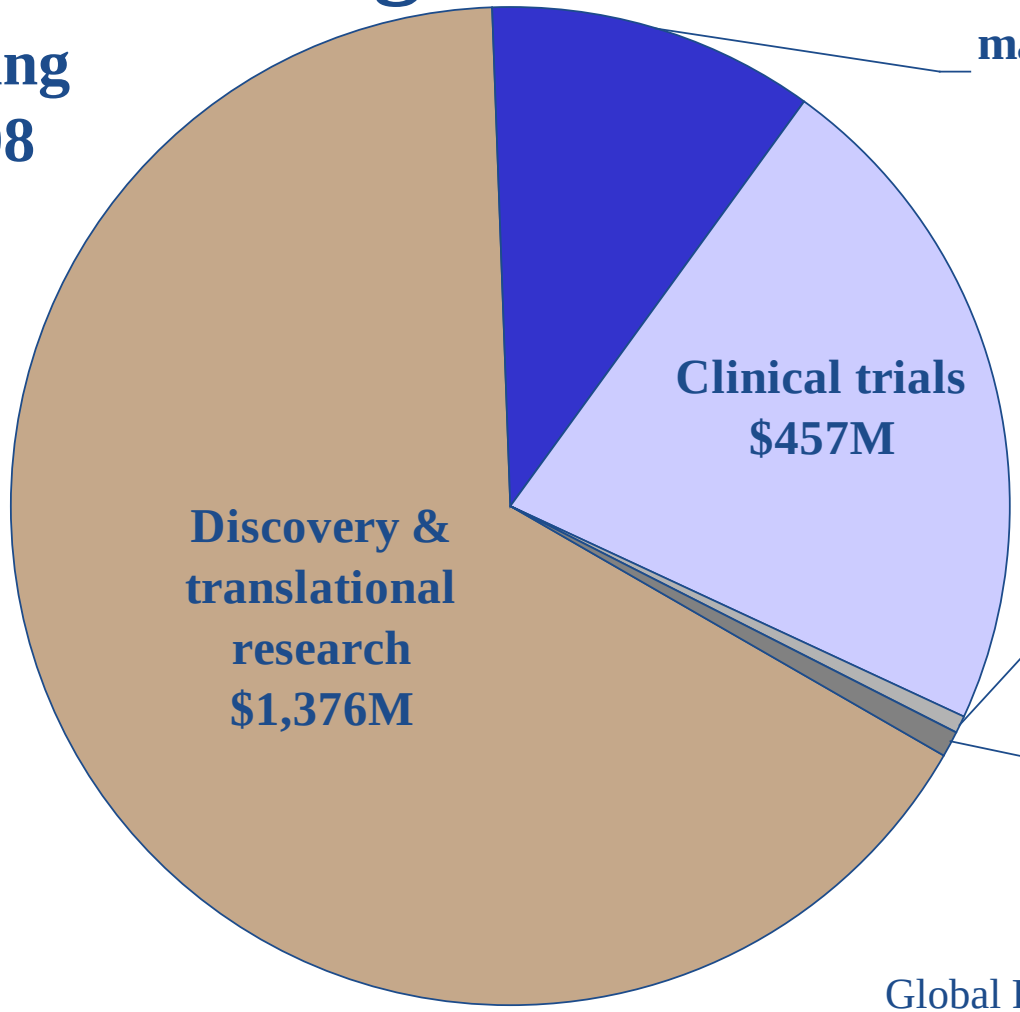
- State-of-the-art immunology and mycobacteriology laboratory established at **India** site, first of the kind in the area for TB diagnosis
- Professional Development Programs established in **Kenya, Uganda** and **India**
- Epidemiological cohort studies initiated in **Kenya** and **Uganda**
- **Kenya**, **Uganda** and **Mozambique** to participate in planned multicountry Phase II trial
- Laboratory capacity being developed in **Kenya** and **Uganda**

Benefits of Site Development and Clinical Research

- Retain local talent and expertise
- Raise awareness about TB in the community
- Support and enhance local clinical research capacity
- Community health and education
- Infrastructure remains in the community
- Leverage investment in infrastructure to use for clinical trials of other diseases

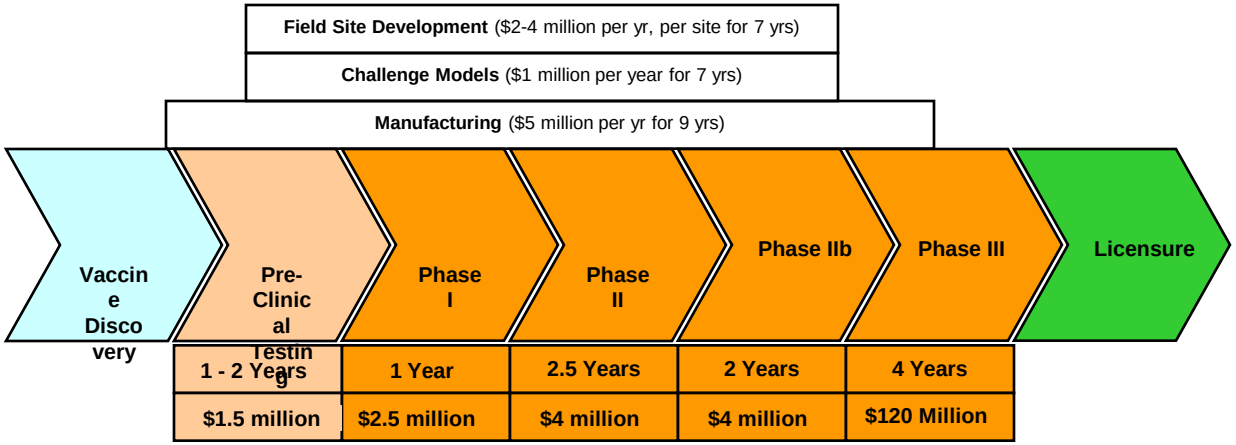
Global TB Vaccine R&D Funding Needs 2006-15

Total funding needs: $2.08 billion



Global Plan to Stop TB, 2006-15

TB Vaccine Development Timeline and Costs



- 4 of Aeras' 6 TB vaccine candidates are in clinical trials in Africa; the others are expected to enter trials in 2009
- $120 million to conduct a Phase III licensure trial of <u>one</u> candidate
- With sufficient resources, a new TB vaccine could be ready by 2016

New TB Vaccines are Global Priority

- New TB vaccines are an important part of a comprehensive strategy to control and eliminate TB as a public health threat
- Aeras and its partners leading effort to develop new TB vaccines
  - Development process for leading candidates identified
  - Field sites and manufacturing being prepared
  - Working with researchers on exciting new concepts in TB vaccine development
- New vaccines need to be a global priority to help ensure rapid development and distribution
- According to Global Plan to Stop TB, $1 billion over the next 10 years is needed to develop new TB vaccines

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Buitenlandse Zaken

Netherlands Ministry of Foreign Affairs

Danida

Ministry of Foreign Affairs of Denmark

CENTERS FOR DISEASE CONTROL AND PREVENTION

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