Tuberculosis Market Assessment; a case for investment in R&D

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Director Global Market Access, Aeras
New Sense of Urgency
Urgent need for new preventative vaccines

Tuberculosis epidemic in the 21st century:

$8 billion a year for TB treatment and care in low and middle income countries alone
We know TB has mutated and evolved

- XDR diagnosed in 77 countries
- Total drug resistant disease reported in India, Iran and Italy
- MDR-TB prevalence will increase by 150% by 2036 without changes to DOTS or DOTS+

(Sez-chuan Suen, 2012, (SMDM))
We have the data and the evidence

Number of MDR-TB* cases estimated to occur among notified pulmonary tuberculosis cases, 2011

MDR-TB cases
- 0–299
- 300–2999
- 3000–29 999
- 30 000–59 999
- ≥ 60 000
- No data
- Not applicable

* MDR-TB: multidrug-resistant tuberculosis (resistance to, at least, isoniazid and rifampicin)


The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
TB VACCINE DEVELOPMENT 2013-2014
Strategies for TB Vaccine Development

Preventive Vaccines: Prime-Boost Regimen

- Improve the prime - recombinant BCG (rBCG) or live *Mtb* vaccine
- Develop novel booster vaccines to extend and enhance immune protection

Immunotherapeutic Vaccines: Boost

- Prevent relapse or reinfection following treatment
- Shorten the course of chemotherapy
# The Global Pipeline of TB Candidates

## 2013

<table>
<thead>
<tr>
<th>PHASE I</th>
<th>PHASE IIa</th>
<th>PHASE IIb</th>
<th>PHASE III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ad5 Ag85A&lt;br&gt;McMaster CanSino</td>
<td>VPM 1002&lt;br&gt;Max Planck, VPM, TBVI, SII</td>
<td>MVA85A/AERAS-485&lt;br&gt;Oxford, Aeras</td>
<td>M. Vaccae&lt;br&gt;Anhui Longcom, China</td>
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<tr>
<td>MTBvac&lt;br&gt;TBVI, Zaragoza, Biofabri</td>
<td>H1 + IC31&lt;br&gt;SSI, TBVI, EDCTP, Intercell</td>
<td>M72 + AS01E&lt;br&gt;GSK, Aeras</td>
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<tr>
<td>ID93 + GLA-SE&lt;br&gt;IDRI, Aeras</td>
<td>RUTI&lt;br&gt;Archivel Farma, S.L</td>
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<tr>
<td>Crucell Ad35/MVA85A&lt;br&gt;Crucell, Oxford, Aeras</td>
<td>H4/AERAS-404 + IC31&lt;br&gt;SSI, Sanofi-Pasteur, Aeras, Intercell</td>
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<td>H56/AERAS-456 + IC31&lt;br&gt;SSI, Aeras, Intercell</td>
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<td>Crucell Ad35/AERAS-402&lt;br&gt;Crucell, Aeras</td>
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- **VIRAL VECTOR**
- **rBCG**
- **PROTEIN/ADJUVANT**
- **ATTENUATED M.Tb**
- **IMMUNOTHERAPEUTIC:** Mycobacterial – Whole Cell or Extract

**AERAS SPONSORED**
TB Vaccine Development: Highlights for 2013-2014

- Phase IIb trial of a new vaccine candidate, M72, to begin enrolment
- Potential to expand to new countries to conduct clinical trials
- New scientific partnerships and collaborations – focus on enabling biomarker and correlate discovery
- Implementation of innovative trial designs – immunotherapy; prevention of infection
TB Market Assessment
## The Economic Impacts of TB

<table>
<thead>
<tr>
<th>FAMILY</th>
<th>COUNTRIES</th>
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<tr>
<td>TB primarily strikes down working-age adults</td>
<td>TB costs the global economy an estimated $1 Billion each day</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>BUSINESS SECTOR</th>
<th>GROWING COST OF DRUG-RESISTANT TB</th>
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<tbody>
<tr>
<td>Annual cost to the South African mining sector is over $880 million</td>
<td>Cost of treatment for MDR - $12,462 per patient in highest burden countries and $250,000 in the U.S.</td>
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<tr>
<td></td>
<td>Hospitalization for one XDR patient - $483,000 in the U.S.</td>
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## Aeras methodology to estimate the market for new TB vaccines

### 1. Defined the global market:
- Disease burden
- TB Incidence by country
- Contact rate of infection
- Impact of HIV status

### 2. Assessed the global market on 3 levels:
- **Product level:**
  - generic TB target product profiles for infants, adolescents & adults were developed
- **Geographic level:**
  Global market segmented into World Bank classifications;
  - High income
  - Middle income
  - Low income
- **Time level:**
  - 10 yr. market revenue horizon
  - 20-30 yr. health impact

### 3. Vetted data and assumptions with partners:
- Academia
- TBVI
- WHO
- Industry experts:
  - GSK
  - Crucell
  - SSI
  - SII
  - Sanofi Pasteur
### TB Vaccines Target Product Profiles

<table>
<thead>
<tr>
<th><strong>Adolescents &amp; Adults Vaccine</strong></th>
<th><strong>Infant Vaccine</strong> (BCG with better efficacy)</th>
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<tbody>
<tr>
<td><strong>Indication</strong></td>
<td>To prevent active disease</td>
</tr>
<tr>
<td><strong>Target Population</strong></td>
<td>≥ 10yo without known active TB</td>
</tr>
<tr>
<td><strong># Doses</strong></td>
<td>2 doses</td>
</tr>
<tr>
<td><strong>Vaccination Strategy</strong></td>
<td>Routine vaccination of 10 yo, and Mass campaigns in ≥ 11yo, every 10 yrs</td>
</tr>
<tr>
<td><strong>Vaccination Coverage Rate Proxy</strong></td>
<td>HPV coverage rate proxy for 10yo</td>
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<tr>
<td><strong>Expected Efficacy</strong></td>
<td>60% improvement in relative efficacy compared to the control arm</td>
</tr>
<tr>
<td><strong>Expected Safety</strong></td>
<td>No safety concerns</td>
</tr>
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<tr>
<td><strong>Newborns independent of HIV status</strong></td>
<td></td>
</tr>
<tr>
<td><strong>1 dose</strong></td>
<td>Routine vaccination of newborns</td>
</tr>
<tr>
<td><strong>BCG</strong></td>
<td></td>
</tr>
<tr>
<td><strong>60% improvement in relative efficacy compared to current BCG</strong></td>
<td>As safe as current BCG</td>
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Conservative Case Assumptions

- 20% coverage rate for adolescents & adults in MICs & LICs
- 90>% coverage rate for infants in MICs & LICs
- HICs coverage rate for sub-populations only:
  - Military 90%
  - Health Care Workers 35%
  - Travelers 35%
  - Children of immigrants 10%
- Steady state vaccination – infants and 10yr. olds in school and not in school
- Mass vaccination campaigns every 10 years; adolescents 10> and adults
- First year of introduction, adolescent & adults, 2024/2030 with WHO pre-qualification; infant vaccine 2030/2033
- Country ramp up to full coverage ranges 2-6 years depending on the population of country

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<tr>
<th>China and India Assumptions</th>
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<tr>
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<tr>
<td><strong>Coverage rate</strong></td>
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<tr>
<td>20% adolescents &amp; adults 90&gt;% infants</td>
</tr>
<tr>
<td><strong>Country Ramp up to full coverage</strong></td>
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<tr>
<td>5 years – adolescents &amp; adults 3 years infants</td>
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Potential Health Impact of New TB New Vaccines

Range of TB Adolescent & Adult Incident Cases Averted

30–50 million TB cases can potentially be averted in adolescents & adults by 2050

An additional 7–10 million TB cases can be averted in infants by 2050

NO VACCINE  VACCINE INTRODUCTION 2024  VACCINE INTRODUCTION 2030

AERAS | Advancing Tuberculosis Vaccines for the World
A minimum of 3 suppliers would be required to meet potential demand within 10 years after vaccine introduction (~250,000 M - 300,000 M)
Overall market revenue potential

HICs & China dominate the market returns

MICs & China dominate the vaccine supply
WORKING WITH THE TB VACCINE FIELD
The TB Vaccine R&D Situation to Date:

So far USD $600M spent and a lot of effort to develop a number of promising TB vaccine candidates in the global portfolio

- **Funding:** Mainly through grants and by some industry for individual candidates.

- **Current Global TB vaccine portfolio:**
  - 12 clinical trials currently underway
  - More than 25 discovery leads and preclinical candidates
  - Efforts to diversify the portfolio underway
  - Lessons learnt from historical trials offer key insights into the biology of tuberculosis informing development efforts
  - Clinical trial capacity and expertise to run large-scale efficacy trials
  - Improved knowledge around biomarkers and correlates of protection informing on vaccine design and animal models
Overview of Possible Funding Solutions

Push Mechanism

**Grants**
- European Commission – EDCTP (Phase 2a)
- Netherlands – DGIS
- UK – DFID
- Bill & Melinda Gates Foundation
- NIH

**Pharma Cost-Sharing**

* Top 5 donors listed provide more than 80% of the funding for TB vaccine R&D globally

Pull Mechanism

**Pharma Cost-Sharing**

- Grant Cost-Sharing
  - EDCTP
  - Donors Channeled through Portfolio Manager

**Market Enhancing Mechanisms**
- Validate the market potential with key EU MS and other HIC/UMIC through a pre-AMC like mechanism utilizing a pre-defined targeted product profile
- Debt finance for the commercial manufacturing scale-up
- Debt finance to governments in support of comprehensive TB vaccination programs
- Establish robust, evidence-based national health economic data to facilitate vaccine adoption
- WHO and national/regional regulatory strategies to facilitate rapid adoption and scale-up
- GAVI & other donors commitment to support
Major Funders and R&D Partners
Thank you.

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