State of the TB Alliance

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Willo Brock
TB Alliance Stakeholders Association Meeting
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Cape Town, South Africa
State of the TB Alliance

2015 Updates

• Vision and Mission

• Program Updates
  – Discovery and clinical development
  – Pediatrics product introduction

• New Initiatives, Partnerships and Stakeholders
Our Vision: Better TB Medicines for All

• Dedicated to the discovery and development of better, faster and affordable TB drugs that are available to **all** who need them

• Achieving *maximum impact* requires:
  – Short, simple regimen that is affordable, available and accessible
  – Universal regimen that is effective in virtually all people with active TB
  – All novel drugs, circumventing challenges of drug resistance
<table>
<thead>
<tr>
<th>LEAD IDENTIFICATION</th>
<th>LEAD OPTIMIZATION</th>
<th>PRECLINICAL DEVELOPMENT</th>
<th>PHASE 1</th>
<th>PHASE 2A</th>
<th>PHASE 2B</th>
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<tr>
<td>Indazoles</td>
<td>Macrolides</td>
<td>Preclinical TB Regimen Development</td>
<td>TBA-354</td>
<td>Linezolid Dose-Ranging Study</td>
<td>NC-005</td>
<td>STAND</td>
<td>Optimized Pediatric Formulations</td>
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<td>Whole-Cell Hit-to-Lead Program</td>
<td>Sanoﬁ</td>
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<td>JHU</td>
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<td>Pretomanid/ Bedaquiline/ Pyrazinamide (BPaz)</td>
<td>Pretomanid/ Bedaquiline/ Linezolid</td>
<td>Ethambutol for children &gt; 5kg</td>
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<td>Whole-Cell Hit-to-Lead Program</td>
<td>GSK</td>
<td>Diarylquinolines</td>
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<td>Isoniazid for children &gt; 5kg</td>
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<td>RNA Polymerase Inhibitors</td>
<td>Rutgers University</td>
<td>DprE1 Inhibitors</td>
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<td>Pyrazinamide for children &gt; 5kg</td>
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<td>AUCK/UIC</td>
<td>MmpI3 Inhibitors</td>
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<td>POA Prodrugs</td>
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<td>PEPCK</td>
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<td>Oxazolidinones</td>
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<td>Hit ID Programs</td>
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<td>IMM</td>
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<td>- Dundee/TAMU</td>
<td>- Pyrimidines</td>
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**TB Alliance R&D Partners:**

- Research Institute (BTTRI)
- Calibr
- Cornell University
- Daichi Sankyo Novare
- GlaxoSmithKline (GSK)
- Institute of Materia Medica (IMM)
- IMPAACT
- Janssen [Johnson & Johnson]
- Johns Hopkins University (JHU)
- Medical Research Council (MRC) at UCL
- OP-BIO
- Roche Pharmaceuticals
- Rutgers University
- Sanoﬁ
- Schrödinger
- Shionogi
- Stellenbosch University
- Sumitomo-Dainippon
- Takeda Pharmaceuticals
- TB Drug Accelerator (TBDA)
- Texas A&M University (TAMU)
- University College London (UCL)
- University of Auckland (AUCK)
- University of Dundee (Dundee)
- University of Illinois at Chicago (UIC)
- University of Pennsylvania School of Medicine (UPenn)
Early-Stage Research: Filling the Pipeline

Optimizing known compound classes

- **TBA-354** Initiated Phase 1 study. First new drug to enter the clinic in six years
- **Oxazolidinone** and **Diarylquinoline** candidates to move into pre-clinical development in 2016

Developing novel classes based on novel targets

- **DprE-1 inhibitor (AZ-7371)** Novel bactericidal compound is approved to move into pre-clinical development
- 2 Lead Optimization and 2 Lead Identification programs initiated

TB Alliance became a full partner in the TB Drug Accelerator Project
MORE new drugs are needed
Progression Toward a Novel Regimen

A fully novel regimen holds potential to treat all forms of TB

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<th>XDR-TB</th>
<th>MDR-TB</th>
<th>DS-TB</th>
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<td>Treatment Potential Using:</td>
<td>1 Novel Drug (PaMZ)</td>
<td>2 Novel Drugs (BPaZ)</td>
<td>3 Novel Drugs (NiX-TB)</td>
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TB ALLIANCE
Nix-TB Clinical Trial

• Nix-TB is the first clinical trial of an XDR-TB regimen with minimal pre-existing resistance
• Tests the combination of BPaOx as a 6-9 month cure that is all pills, no injections
• Testing safety of linezolid
• More than 25 patients enrolled; First participant with XDR-TB completed six-month study treatment in November
• Regimen could be first “universal” treatment

A 2014 Lancet study found nearly half of XDR-TB patients died within a year of diagnosis.
Advancing TB Medicines for Children

Preparing for FDC Introduction

New childhood medicines can improve treatment and save lives

• Now available
• Accurately dosed, quality-assured, child-friendly TB medicines; first time since WHO changed guidelines in 2010
• Affordable treatment; Commitment from two manufacturers
• Working with partners to facilitate uptake and adoption: WHO, UNITAID, USAID, UNICEF, MSH, GDF, Global Fund and others
A Global Network of Partners

Leveraging the best science from around the world
Stakeholder Perception Survey

- Conducted November 2014
- 84% rate their experience with TB Alliance as good or very good
- 78% of respondents rate their experience with TB Alliance as similar to or better than other PDPs; only 8% rate their experience as worse than other PDPs
- 69% rate TB Alliance as effective in developing new drugs that will significantly help to address the pandemic
- 81% rated the importance of TB Alliance being involved along the entire spectrum of TB-related activities as important
Expanding partnerships

TB Alliance saw the development of several exciting partnerships

- Research partnerships: (Re)engagement in early research
- Stakeholders
- Manufacturers and delivery partners
- Communities and patients
- Advocacy and policy collaboration
TB Alliance Supporters

- Australian Department of Foreign Affairs and Trade
- Bill & Melinda Gates Foundation
- European Commission
- United States Food and Drug Administration
- Global Health Innovative Technology Fund
- Indonesian Health Fund
- Irish Aid
- US NIAID
- UK aid
- UNITAID
- United States Agency for International Development
Thank you!