Partnerships in the Age of Bedaquiline: Successes, Challenges and the Beginning of the End of TB

Combating Antimicrobial Resistance: A One Health Approach to a Global Threat – A Workshop
NAS, Washington, DC
21 June 2017
GPH Bridges Business and Philanthropic Domains

Core Business
Sector-specific product- and solution-centric innovations that improve patient / consumer outcomes and deliver financial return via market / commercial channels

Global Public Health
Cross-sector product- and solution-centric innovations that improve patient / social outcomes in resource-poor settings via sustainable access models / partnerships

Global Community Impact
Social impact innovation that seeks to strengthen the humans at the frontlines of care and sustain healthy communities

Healthcare Company of the Future
Leveraging transformational technology to achieve high aspirations

Core Focus Areas

A world unburdened by tuberculosis

A world unburdened by HIV

Unprecedented, sustainable outcomes for those living with mental illness

Improved child health & development through soil transmitted helminth elimination

Supporting Platforms & Other Areas of Interest

Vaccines

Global Health Security

Global Surgery
Discovery Timeline for TB Drugs

- **1921**: BCG Vaccine discovered
- **1946**: 1st antimycobacterial discovered (streptomycin)
- **1952**: Isoniazid discovered
- **1965**: Rifampin* discovered

*No New TB drugs with a new mechanism of action since Rifampin*
Drug Resistant TB (RR + MDR)

Of the 580,000 incident cases per year
- Missing 34%
- Deaths 43%
- Diagnosed 23%
- Untreated 78%
- Treated 22%
- Cured 52%
- Not cured 48%
- RR+MDR 88%

Less than ¼ are treated
Approximately one-half of those treated are cured
Less than 12% are cured

90% of cases spread drug-resistant TB by a simple cough

Source: WHO Global Tuberculosis Report 2016
# Bedaquiline (BDQ)

<table>
<thead>
<tr>
<th><strong>Target Patient Population</strong></th>
<th>Adults (18 and over) patients with diagnosed pulmonary MDR-TB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism of Action</strong></td>
<td>ATP synthase inhibitor</td>
</tr>
<tr>
<td><strong>Usage</strong></td>
<td>Part of combination therapy for adults (18 and over) with pulmonary drug resistant tuberculosis. Typically added to a standard of care regimen comprised of 5-7 drugs.</td>
</tr>
</tbody>
</table>
| **Dosing**                    | 400mg daily for initiation period of 2 weeks  
200mg three times weekly - maintenance period of 22 weeks |
| **Formulation**               | Oral                                                        |
| **Shelf life**                | 36 months                                                  |
WHO Interim Guidelines: 2016 Review

Reserved for adult MDR patients not eligible for WHO short regimen. Includes patients with resistance or intolerance to FQ or injectables…and XDR patients ~ 30% of the MDR patient pool


Global: 580,000 incident cases
Treated: 125,000
BDQ eligible patients: 37,500

“…part of a combination therapy of at least three drugs in adults with pulmonary MDR-TB…”

FDA: U.S. Food and Drug Administration; MDR-TB: multidrug resistant tuberculosis; PI: prescribing information; XDR-TB: extensively drug-resistant tuberculosis; WHO: World Health Organization; ¹ WHO 2013
TB: A Case for Collaboration

Constrained funding

Weak healthcare delivery systems

Limited diagnostic capacity

Patient population with limited resources

Poor prescribing / adherence practices

No sense of urgency

Bedaquiline enables improvement of the MDR-TB standard of care

Inadequate Standard of Care
Bedaquiline: At Heart of Collaboration in Combatting DR-TB
Regulatory Status: May 2017

Submitted for Registration:
- Vietnam
- Colombia
- Thailand
- Indonesia
- Turkey
- Mexico
- Belarus
- Bangladesh
- Japan
- Burundi
- Ghana
- Kenya
- Rwanda
- Tanzania
- Uganda

High Burden MDR cases:
70%
- South Korea
- South Africa
- Peru
- Philippines
- Turkmenistan
- Macau
- New Zealand
- Taiwan
- Moldova

8%
- Vietnam
- Colombia
- Thailand
- Indonesia
- Turkey
- Mexico
- Belarus
- Bangladesh
- Japan
- Burundi
- Ghana
- Kenya
- Rwanda
- Tanzania
- Uganda
South Africa: Tackling DR-TB - Sustained Investments, Diverse Partners

- e-health platforms
- Portable audiometers
- Patient brochures
- Data management
- MDR-TB registry
- Advisory Boards
- HCW Training
- Antibacterial surveillance
- Disease awareness
- Website (whatistb.com)

“... Treatment outcomes in Pre/XDR TB are now overtaking our outcomes in MDR-TB: New Drugs are a top priority.”
India: Beyond the Pill

HCP Training & Collaboration

**Physician Education**
- Expand on existing collaboration with Maharashtra State Anti-TB association for training of primary care providers in management of TB
- Collaboration with UNION to conduct 24 DRTB and 80 TB clinical management training programs across 24 high disease burden cities across India
- HCP training for expansion of sites (2 workshops)

Patient Support

**Nutrition Projects**
- 13 Nutrition projects run across the country – 5,000 TB Patients (4,000 MDR-TB) patients provided with nutrition support.
- All 6 CAP sites part of the project; Besides other high burden states being supported
- Implementing institutions/NGOs – National Institute of Research in TB (NIRT), Doctors For You (DFY), TB Alert and Alert India

Advocacy & Awareness

- Municipal corporations collaboration (in high burden states) over 3 years - mass transit drives, community awareness drives in slums, mass media, advocacy efforts with journalists & elected officials
- PATH collaboration on community awareness videos for use in clinics
- RNTCP collaboration to support community TB ambassadors in slums and other high risk populations, and provide IEC material

Case Detection & Stakeholder Collaboration

- Project Oyster – ~30K new TB patients and ~5K MDR-TB diagnosed across 10 high epidemic zones
- Project Sunshine – 50,000 symptomatic mine workers screened for TB and linked up for treatment to local DOTS centers
- 20,000 Diagnostic tests provided free of cost to symptomatic patients in Mumbai in Non Public segment (PPIA project)
- High priority National and state level collaborations
China: Controlled Access Program

Oversight Board:
- Bill & Melinda Gates Foundation
- Xian Janssen
- China Primary Healthcare Foundation

Program Owner:
- CCTB

Site selection
- System
- Scale-up
- Local funding
- Oversight

PV
- Dx algorithm
- HCP training
- Evaluation
- Community

Drug
- Data generation
- Med Ed
- Patient support

Partners:
- China Primary Healthcare Foundation
- FHI 360
- CDC
Four-year program

Up to 30,000 treatments for eligible patients

Over 100 low and middle income eligible countries

Global Fund eligibility criteria

Appropriate use in accordance with WHO Guidelines

Insights into real world use
## Bedaquiline Donation Program

### Roles & Responsibilities

<table>
<thead>
<tr>
<th>Role</th>
<th>Responsible Parties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory</td>
<td>Janssen</td>
</tr>
<tr>
<td>Distribution</td>
<td>USAID</td>
</tr>
<tr>
<td>Technical Assistance</td>
<td>Janssen, USAID, and</td>
</tr>
<tr>
<td>Medical Information/ Medical Education</td>
<td>Janssen, USAID, and</td>
</tr>
<tr>
<td>Pharmacovigilance</td>
<td>USAID, Janssen, and</td>
</tr>
<tr>
<td>Monitoring &amp; Reporting</td>
<td>USAID</td>
</tr>
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</table>
Bedaquiline Treatments: > 19,000 patients in over 80 countries*

Source: http://drtb-stat.org/global-snapshot/

* Through end May 2017
Bedaquiline: Accelerator for Addressing AMR

**Technology**

- Bedaquiline: First novel mechanism of action in 40+ years; comprehensive access strategy in place
- New tools under development with bedaquiline as foundation
  - Shorter regimens
  - New platforms
  - Novel targets

**Infrastructure**

- WHO Global guidelines for antibiotic stewardship
- Partnership with Global Drug Facility for controlled distribution
- Investments in surveillance & detection
- Health systems capacity building & education

**Expanding Impact**

- Transformational potential in XDR & MDR-TB
- Building robust health systems & unlocking healthcare system capacity
- Creating a blueprint for addressing AMR in developing countries -- estimated to have a 2.3%-3.5% impact on global GDP by 2050
Currently No Pull Incentives and Market Failure
Fostering a Healthy AMR Ecosystem

Build on existing structures and concepts
Networked solution with academia, governments and industry
Introduce risk-sharing mechanism for drug development
Market entry awards or incentives for innovators
Equitable procurement mechanism to ensure sustainability of funding and manufacturing
Structure for stewardship and post approval support

Additional tools for solving the AMR challenge
Using learnings from bedaquiline development & access efforts to inform creation of new tools

**Clinical Evaluation** – Leveraging BDQ registry and other infrastructure for faster evaluation

**Regulatory** – Building faster approval pathway in key markets (which can be challenging outside of Europe/US); finding was to share costs of post approval commitments

**Manufacturing** – Forecasting for low-volume manufacturing challenging: using BDQ roll-out experience to improve predictions

**Appropriate Use / Access** – Taking advantage of existing market access strategy / programs for faster roll out
Novel tools & regimens needed to “turn off the tap” of TB

Prophylactic vaccine

Long acting Delivery platform

Effective, short-course fixed-dose combo, low toxicity

All oral short course (e.g., 6 month); ideally fixed-dose combo

Highly effective salvage therapy

Uninfected → Latent TB → Active TB → MDR TB → XDR TB → Death

Possibly one single “pan-TB” regimen

Bedaquiline today: part of 24 month course

XDR = Extensively Drug Resistant  MDR = Multidrug Resistant; Usage in XDR vs. MDR varies by country
More than 2 Billion People with Latent TB: What is the Strategy?

A World Free of the Burden of TB

Without accelerated discovery, development, and deployment of new tools and technologies, this aspiration is not achievable