Bedaquiline

CPTR TB Drug Development Roundtable

Sep 24, 2012

Chrispin Kambili, M.D.
Bedaquiline Development Program


Non-clinical

Phase I

11 trials

- C202, 75 pts
- C208 Stage 1, 47 MDR-TB pts

Phase II

- C208 Stage 2, 160 MDR, pre-XDR-TB pts
- C209, 233 MDR, pre-XDR, XDR-TB pts

EAP/CU/ATU

>500 patients

Phase III

STREAM

Pediatric PK Study

C211

Phase IV

Multi-country Registry

Janssen

Pharmaceutical Companies of Johnson & Johnson
Early access/expanded access programs

ATU in France

Global Compassionate Use Program

EAP Trial in Russia and Lithuania

Early or Expanded Access

All 3 limited to (pre) XDR TB
Numbers of patients who have received bedaquiline in compassionate use programs, 2011-2014

Top 5 Countries (cumulative):

- South Africa: 127
- France: 107
- Armenia: 47
- Georgia: 36
- Latvia: 35

Total=487, as of Sept 1)
Cumulative reported deaths in *on-going* expanded access programs, 2011-2014

<table>
<thead>
<tr>
<th>Program</th>
<th>Number exposed to bedaquiline</th>
<th>Cumulative number of deaths reported</th>
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<tbody>
<tr>
<td>Global Compassionate Use program</td>
<td>380</td>
<td>7</td>
</tr>
<tr>
<td>ATU Program in France</td>
<td>107</td>
<td>5</td>
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<tr>
<td>EAP Trial (Russia and Lithuania)</td>
<td>57</td>
<td>2</td>
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</tbody>
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Source: Janssen Safety Database  
Data as of Sept 1, 2014
Phase III: STREAM Stage 2 Trial Design

N = 1,155 MDR-TB patients
Pediatric PK/Safety: Sequential Age Group Approach

Pulmonary MDR-TB, pre-XDR-TB: N at least 60

- Adolescents (12-<18 y): Tablets preferred
- Older Children (5-<12 y): Tablets acceptable
- Toddlers & Young Children (2-<5 y): Age appropriate & convenient dosing formulation preferred
- Infants and toddlers (birth-<2 y): Age appropriate & convenient dosing formulation preferred

Intensive PK interim analyses of cohorts

FPI: Q1 2015
• Describe BDQ drug utilization data:
  – Indication, dose/duration, and type of treating site

• Describe adverse events among BDQ-treated patients, including deaths

• To compare the treatment outcomes between BDQ-treated patients and patients not treated with BDQ

• *Countries targeted as ‘early adopters’: South Africa, Vietnam, Philippines, Indonesia, Korea, Peru*

• *FPI: Q1 2015*

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*A public / private collaboration to track the introduction and use of bedaquiline and to capture treatment outcomes*
Regulatory update

APPROVALS

<table>
<thead>
<tr>
<th>Region</th>
<th>Date</th>
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<tbody>
<tr>
<td>US (Accelerated approval)</td>
<td>Dec 2012</td>
</tr>
<tr>
<td>Russia*</td>
<td>Oct 2013</td>
</tr>
<tr>
<td>EU (Conditional Approval)</td>
<td>Mar 2014</td>
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<tr>
<td>South Korea (Orphan drug)</td>
<td>Mar 2014</td>
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Regulatory dossiers filed in:

<table>
<thead>
<tr>
<th>Region</th>
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<tbody>
<tr>
<td>China</td>
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<tr>
<td>South Africa</td>
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<td>Colombia</td>
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<td>Vietnam</td>
<td>Turkmenistan*</td>
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<tr>
<td>Peru</td>
<td>Uzbekistan*</td>
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*Dossier submitted by Pharmstandard
Our ‘asks’ from CPTR

• Continue broad and inclusive engagement of ALL stakeholders
  – Encourage support for all activities of global public health benefit

• Provide a platform that allows objective appraisal and alignment of studies to ensure that limited resources for TB drug research are optimally utilized for the greater good:
  – duplicative efforts should be discouraged
  – scientific rigor should be paramount when framing research questions

• Help identify ways to align regulatory requirements with public health needs for new tools for TB control
Thank you!