Overview

• Progress in clinical development
  • Phase 3 trial Update
  • Pediatric trial Update

• Update on regulatory progress

• Additional activities
  • DDI studies
  • Public health advocacy and education
Trial 213 Update

Randomised, Blinded, Confirmatory Study

Trial 213 (On-going)

- 6 mo. OBR* + delamanid or placebo
- 12-18 months OBR
- 6-12 mo. follow-up

Completed November 2013
IMP Completed May 2014

LPLV May 2016

<table>
<thead>
<tr>
<th>Region</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>511</td>
<td>-</td>
</tr>
<tr>
<td>Philippines</td>
<td>127</td>
<td>25%</td>
</tr>
<tr>
<td>Baltics and Moldova</td>
<td>126</td>
<td>25%</td>
</tr>
<tr>
<td>Peru</td>
<td>157</td>
<td>31%</td>
</tr>
<tr>
<td>South Africa</td>
<td>101</td>
<td>20%</td>
</tr>
<tr>
<td>HIV+ and Treated with ARV</td>
<td>48</td>
<td>9%</td>
</tr>
<tr>
<td>Treated with moxifloxacin</td>
<td>121</td>
<td>24%</td>
</tr>
</tbody>
</table>

* OBR: Optimised Background Treatment Regimen
Pediatric Program Update

**Trial 232: Phase 1 PK Age De-escalation study**
Define dose of delamanid in children resulting in AUC comparable to the effective AUC observed in adult MDR-TB trials

**Trial 233: Phase 2 Safety Study**
Investigate the safety, tolerability, and PK of delamanid administered for six months in a pediatric population receiving concomitant OBR

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Trial 232 Status</th>
<th>Trial 233 Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-17 years old</td>
<td>7 enrolled/ 7 completed</td>
<td>7 enrolled/ 7 completed</td>
</tr>
<tr>
<td>6-11 years old</td>
<td>5 enrolled/ 3 completed</td>
<td>2 enrolled/ 0 completed</td>
</tr>
<tr>
<td>3-5 years old</td>
<td>Start April 2015</td>
<td>Start May 2015</td>
</tr>
<tr>
<td>0-2 years old</td>
<td>Start August 2016</td>
<td>Start August 2017</td>
</tr>
</tbody>
</table>

**Bioequivalence Study for Pediatric Formulation**
- Patients enrolled 8 September
- Results available Q1 2015 to support enrollment of Cohort 3-5 year old children
Delamanid Regulatory Submissions and Approvals

• Approval received in the EU from the EMA 28 April 2014

• Approval received in Japan from the MHLW 4 July 2014

• Submission made to the WHO for policy guidance and review is in process

• Future submissions and other access strategies to be prioritized in countries where delamanid clinical trials conducted
Additional Activities

• **Delamanid – Bedaquiline DDI Study**
  - ACTG 5343 will study drug-drug interactions with co-administration of bedaquiline and delamanid in the treatment of MDR-TB with a focus QT interval prolongation
  - Projected launch in Q1 2015

• **Compassionate Use**
  - **Individual Requests**: Physician request for individual patient reviewed by WHO/ERS Consilium, Otsuka CU Committee, ethics board of institutions and local regulatory bodies
    STATUS: Active, ongoing
  - **Collaboration with MSF**: CU program administered by MSF in select countries for fixed number of patients
    STATUS: Awaiting final approval from local authorities