ABX464 is a first-in-class antiviral drug candidate for the treatment of patients with HIV infection. It is an orally available small molecule that blocks HIV replication through an entirely novel mechanism, inhibition of Rev activity.

Preclinical data in humanized mice showed that ABX464 monotherapy had an antiviral effect, which was sustained after treatment interruption. A prior food-effect study demonstrated a 3-fold increase in parent drug exposure when administered with food without a significant impact on the active glucuronide metabolite.

**Objectives**

- Evaluate pharmacokinetics and viral kinetics of ABX464 in untreated patients with HIV infection.

**Primary endpoint:**

- To evaluate the safety and tolerability of repeated oral administrations of ABX464.

**Secondary endpoint:**

- To evaluate pharmacokinetics and viral kinetics of ABX464 in untreated patients with HIV infection.

**Methods**

- Four centers in Thailand and one in Mauritius were included in the study and conducted local ethics reviews.
- Patients were enrolled after confirmation of HIV infection and no history of prior antiretroviral therapy.
- Patients were randomized into successive cohorts of 8 patients where 6 received 14 or 21 days of ABX464 and 2 received placebo.
- Dose escalation calculations were validated by an independent Data Safety Monitoring Board (DSMB).
- The initial group received 25 mg every 3 days. Successive groups received 25, 50, 75, 100, and 150 mg QD. The 25, 50, and 100 mg groups took drug fasting for 21 days, the 75 and 150 mg groups took drug with food for 14 days.

**Results**

- The most common adverse events noted were headache, nausea, and vomiting.
- All events were grade 1 or 2.
- All patients completed at least 14 days of treatment per protocol.
- There were no serious adverse events.

**Table 2. Most Frequent Adverse Events (>10%) by Group**

<table>
<thead>
<tr>
<th>Group</th>
<th>Placebo (n=8)</th>
<th>150 mg QD, fasting (n=6)</th>
<th>75 mg QD, fasting (n=6)</th>
<th>50 mg QD, fasting (n=2)</th>
<th>25 mg QD, fasting (n=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>7 (87.5)</td>
<td>1 (16.7)</td>
<td>3 (50.0)</td>
<td>1 (50.0)</td>
<td>1 (50.0)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1 (12.5)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (12.5)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

**Table 3. Correlation of ABX464 vs Adverse Event Incidence**

<table>
<thead>
<tr>
<th>Method</th>
<th>Max of Cmax vs Average of Cmax</th>
<th>Cmax vs Number of AEs</th>
<th>Spearman Correlation Coefficient (95% CI)</th>
<th>Cmax vs Duration of AEs</th>
<th>Spearman Correlation Coefficient (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVG</td>
<td>0.58 (0.16 to 0.89)</td>
<td>0.16 (0.29 to 0.89)</td>
<td></td>
<td>0.63 (0.24 to 0.92)</td>
<td></td>
</tr>
<tr>
<td>MAX</td>
<td>0.57 (0.31 to 0.86)</td>
<td>0.62 (0.31 to 0.92)</td>
<td></td>
<td>0.57 (0.31 to 0.92)</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion**

- ABX464 was well tolerated in this first in study in treatment-naive HIV-infected patients.
- The most common drug-related adverse events were headache, nausea, and vomiting. All occurred within the first 24 hours of dosing and diminished; no event was greater than grade 2.
- Preliminary PK analysis suggest these events are related to Cmax.
- ABX464 monotherapy showed dose-related antiretroviral activity of 4-6 patients in the 150 mg dose group achieving 0.5 log10 reduction by Day 14. Preliminary PK analysis does not differentiate responders versus non-responders.
- These results warrant the further planned development of this novel acting antiretroviral drug.

**References**

3. ACKNOWLEDGEMENTS
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