The inclusion of the QR code on your

Subjects were followed for a minimum of 28 days after last day of

• TXL 5, 10, 25, 50, and 100 mg orally administered for 28 days to

• Tenofovir exalidex (TXL) is a novel prodrug of the acyclic
nucleotide phosphonate tenofovir (TFV). By chemically

dose study (CTRV-CMX-102) reported favorable safety,
circulating levels of TFV, thereby reducing the potential for

renal and bone side effects. A single dose rat study of 20mg/kg

TXL with an 86% first pass liver extraction demonstrated

extensive liver targeting. The phase 1 multiple ascending oral
dose study was designed to investigate safety, pharmacokinetics and

HBV antiviral effects of TXL.

INTRODUCTION

Pharmacokinetics, Safety and Antiviral Activity of Tenofovir Exalidex (TXL™), a Novel Prodrug of Tenofovir, Administered as Ascending Multiple Doses to HBV-Infected Subjects: A 28 Day Study Final Analyses

Tawesak Tanwandee 1, Satawat Thongsawat 2, Wattana Sukeptaisarnjaroen 3, Pisit Tangkijvanich 4, Piyawat Komolmit 5, Anchalee Avihingsanon 5, Teerha Piravisuth 7

MATERIAL & METHODS

• Phase 2 study for the safety, tolerability, pharmacokinetics and antiviral activity in HBV-infected subjects,

• TXL 5, 10, 25, 50, and 100 mg orally administered for 28 days to sequential cohorts of 12 treatment naive HBV-infected subjects randomized 10:2, TXL: Viread®.

• Subjects were followed for a minimum of 28 days after last day of dosing.

• Sixty-two subjects were enrolled in the study, sixty-one subjects completed. One subject was discontinued for not meeting an inclusion criterion.

Baseline Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>2 mg</th>
<th>5 mg</th>
<th>10 mg</th>
<th>25 mg</th>
<th>50 mg</th>
<th>100 mg</th>
<th>5 mg</th>
<th>10 mg</th>
<th>25 mg</th>
<th>50 mg</th>
<th>100 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Viread® (office)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose (mg)</td>
<td>2.0</td>
<td>5.0</td>
<td>10.0</td>
<td>25.0</td>
<td>50.0</td>
<td>100.0</td>
<td>5.0</td>
<td>10.0</td>
<td>25.0</td>
<td>50.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Efficacy (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tai 1 (%)</td>
<td>1.1</td>
<td>4.5</td>
<td>6.1</td>
<td>6.4</td>
<td>11.0</td>
<td>4.8</td>
<td>11.0</td>
<td>4.8</td>
<td>6.1</td>
<td>6.4</td>
<td>11.0</td>
</tr>
<tr>
<td>Tai 2 (%)</td>
<td>2.5</td>
<td>9.0</td>
<td>6.4</td>
<td>9.1</td>
<td>13.8</td>
<td>7.3</td>
<td>13.8</td>
<td>7.3</td>
<td>9.1</td>
<td>13.8</td>
<td>7.3</td>
</tr>
<tr>
<td>Tai 3 (%)</td>
<td>20.2 (0.0)</td>
<td>21.0 (2.1)</td>
<td>23.3 (2.1)</td>
<td>21.7 (1.8)</td>
<td>21.3 (2.9)</td>
<td>22.9 (2.3)</td>
<td>21.0 (2.1)</td>
<td>23.3 (2.1)</td>
<td>21.7 (1.8)</td>
<td>21.3 (2.9)</td>
<td>22.9 (2.3)</td>
</tr>
<tr>
<td>Tai 4 (%)</td>
<td>40.0</td>
<td>103 (94)</td>
<td>47 (34)</td>
<td>91 (76)</td>
<td>69 60</td>
<td>58 (23)</td>
<td>47 (34)</td>
<td>60 69</td>
<td>58 (23)</td>
<td>47 (34)</td>
<td>60 69</td>
</tr>
<tr>
<td>Tai 5 (%)</td>
<td>6.33 (1.1)</td>
<td>6.06 (1.11)</td>
<td>6.07 (0.26)</td>
<td>5.97 (0.35)</td>
<td>5.39 (0.27)</td>
<td>5.01 (0.52)</td>
<td>6.33 (1.1)</td>
<td>6.06 (1.11)</td>
<td>6.07 (0.26)</td>
<td>5.97 (0.35)</td>
<td>5.39 (0.27)</td>
</tr>
<tr>
<td>Mean ± SD (min, max)</td>
<td>22.0</td>
<td>33.1</td>
<td>33.9</td>
<td>29.3</td>
<td>36.0</td>
<td>18.1</td>
<td>33.1</td>
<td>33.9</td>
<td>29.3</td>
<td>36.0</td>
<td>18.1</td>
</tr>
</tbody>
</table>

• Mean Tₚₑₜ ranged from 3.0 to 6.0 hours.

• Metabolite ½ₚₑₜ values were notably longer than parent drug values.

• Trough Cᵥ levels and AUCs for TFV increased with escalating TXL dose and were consistent with modest accumulation of TFV at steady state.

• Accumulation ratio ranges from 1.48:1 to 1.95 and increased with dose.

RESULTS

Number of Subjects with AEs by SOC

<table>
<thead>
<tr>
<th>SOC</th>
<th>2 mg</th>
<th>5 mg</th>
<th>10 mg</th>
<th>25 mg</th>
<th>50 mg</th>
<th>100 mg</th>
<th>5 mg</th>
<th>10 mg</th>
<th>25 mg</th>
<th>50 mg</th>
<th>100 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• No non-responders.</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>9</td>
<td>10</td>
<td>21</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>• There were no AEs leading to study drug discontinuation, no SAEs, and no deaths during the study. Results are consistent with the disease and the study population.</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>9</td>
<td>10</td>
<td>21</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>• There were no AEs leading to study drug discontinuation, no SAEs, and no deaths during the study. Results are consistent with the disease and the study population.</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>9</td>
<td>10</td>
<td>21</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>9</td>
<td>10</td>
</tr>
</tbody>
</table>

CONCLUSIONS

• TXL was safe and well tolerated when administered fasted to HBV-infected subjects at 5, 10, 25, 50, and 100 mg PO QD for 28 days.

• Systemic exposure, Cmax, AUCs, for TXL and TFV in fasted subjects increased with escalating TXL dose for both single and repeated daily doses of TXL.

• There were no AEs leading to study drug discontinuation, no SAEs, and no deaths during the study. There were no dose-related or other patterns observed in the types, frequency or severity of AEs.

• The magnitude of viral load reduction in the TXL dosing groups was dose-dependent and comparable to that seen in the TDF dosing group.

• Lower systemic circulating TFV levels may mitigate bone and kidney toxicities previously reported for Viread®.

• First generation prototype formulation is now being optimized to enhance pharmacological properties.

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Thank you,
Study Subjects
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