Plasma Pharmacokinetics of Single- and Repeat-Dose Intravitreal EYP-1901 (Vorolanib in DURASERT®) in Rabbits Over 12 Months

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Background

• Vorolanib is a pan-VEGFR inhibitor
• Tyrosine kinase inhibitors (TKIs) are widely used
• Intravitreal anti-VEGF therapy for wet age-related macular degeneration (wAMD)2-5:

Results

Figure 1: Chemical Structure of Vorolanib

Figure 2: Vorolanib Strongly Binds and Inhibits VEGFR2

Table 1: Dosing Groups and Treatments

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose</th>
<th>Regimen Type</th>
<th>Dose at Day 1</th>
<th>Dose at Day 120 (Month 4)</th>
<th>AUCt1-t2, μg · h/L</th>
<th>Cmax, ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0 μg</td>
<td>Repeat dose</td>
<td>0 μg (placebo)</td>
<td>0 μg (placebo)</td>
<td>0 μg</td>
<td>0 μg</td>
</tr>
<tr>
<td>2</td>
<td>2576 μg</td>
<td>Repeat dose</td>
<td>1288 μg</td>
<td>1288 μg</td>
<td>1 sham injection</td>
<td>1 sham injection</td>
</tr>
<tr>
<td>3</td>
<td>3863 μg</td>
<td>Repeat dose</td>
<td>2576 μg</td>
<td>1288 μg</td>
<td>No injection</td>
<td>No injection</td>
</tr>
<tr>
<td>4</td>
<td>1288 μg</td>
<td>Single dose</td>
<td>1288 μg</td>
<td>NA</td>
<td>2 shams injections</td>
<td>NA</td>
</tr>
<tr>
<td>5</td>
<td>2576 μg</td>
<td>Single dose</td>
<td>2576 μg</td>
<td>NA</td>
<td>No injection</td>
<td>NA</td>
</tr>
</tbody>
</table>

• Plasma exposures were consistently maintained below IC50 for VEGFR2 after single and repeat dose administration.
• EYP-1901 provides rapid and sustained levels of vorolanib over a 12-month period after single and repeat dose administration.
• No evidence of saturation or accumulation after repeat dosing (Figure 3B).

Conclusions

• EYP-1901 provides rapid and sustained levels of vorolanib over a 12-month period after single and repeat dose administration.
• Plasma exposures were generally consistent and dose proportional (Table 2).
• Vorolanib levels were below half-maximal inhibitory concentration (IC50) for VEGFR2 throughout 12 months for both single and repeat injections (Figure 3A, 3B).
• No evidence of saturation or accumulation after repeat dosing (Figure 3B).

References:

Please visit eyepointpharma.com for more information.

Dr. Kuppermann acknowledges an unrestricted grant from Research to Prevent Blindness to the Gavin Herbert Eye Institute. Medical writing services were provided by Elizabeth Kukielka, PharmD, of Two Labs Pharma Services.

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