In healthy subjects, pexidartinib was given as a single oral dose of 200 mg to 2400 mg, and the pharmacokinetics were characterized. The lower limit of quantification (LLOQ) of pexidartinib was 2.5 ng/mL in study PLX108-01, with a total of 422 subjects contributing to the analysis.

### Data Source and Study Design

Data were from 12 clinical studies with a total of 422 subjects who contributed to this analysis, including three additional studies with Asian patients. The studies included in the previous pooled population PK analysis are summarized in Table 1.

### Subjects

**Population PK Analysis**

- **Pexidartinib structural model**
  - The structural PK model was a two-compartment model with sequential zero- and first-order absorption and lag and linear elimination from the central compartment.
  - Individual variability was included on clearance from central compartment (CL), inter-compartmental clearance (Q), and absorption rate constant (Ka).
  - The fraction of pexidartinib formation was fixed to 1 in the model, which represented the fraction of pexidartinib dose to form the metabolite ZAAD-1006a.
  - It was fixed to 0.25 based on results from the in vitro balance analysis F(207)-H(115).

### RESULTS

- Observed concentrations of pexidartinib and ZAAD-1006a in Asian and non-Asian patients were within the overall concentration range in all subjects (Figures 1 and 2).

### REFERENCES


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**Table 1. Summary of Subject Demographic and Baseline Characteristics**

<table>
<thead>
<tr>
<th>Race</th>
<th>n (%)</th>
<th>Total Number of Subjects</th>
<th>Median (P5−P95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian</td>
<td>62</td>
<td>333</td>
<td>2.5 (2.0, 3.0)</td>
</tr>
<tr>
<td>Non-Asian</td>
<td>202</td>
<td>721</td>
<td>2.5 (2.0, 3.0)</td>
</tr>
</tbody>
</table>

---

**Table 2. Summary of Studies Included in the Updated Population PK Analysis**

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of PK Samples</th>
<th>Number of ZAAD-1006a PK Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLX108-01</td>
<td>1122</td>
<td>3828</td>
</tr>
<tr>
<td>PLX108-13</td>
<td>1122</td>
<td>3828</td>
</tr>
<tr>
<td>ZAAD-1006a</td>
<td>300</td>
<td>1000</td>
</tr>
<tr>
<td>Total</td>
<td>263</td>
<td>1066</td>
</tr>
</tbody>
</table>

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**Table 3. Summary of Studies Included in the Previous Population PK Analysis**

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of PK Samples</th>
<th>Number of ZAAD-1006a PK Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLX108-01</td>
<td>200</td>
<td>600</td>
</tr>
<tr>
<td>PLX108-13</td>
<td>200</td>
<td>600</td>
</tr>
<tr>
<td>ZAAD-1006a</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>Total</td>
<td>500</td>
<td>1400</td>
</tr>
</tbody>
</table>

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**Table 4. Comparison of Pexidartinib and ZAAD-1006a (ZAAD-1006a) between Asian and Non-Asian Patients**

<table>
<thead>
<tr>
<th>Race</th>
<th>Median (P5−P95)</th>
<th>Median (P5−P95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian</td>
<td>2.5 (2.0, 3.0)</td>
<td>2.5 (2.0, 3.0)</td>
</tr>
<tr>
<td>Non-Asian</td>
<td>2.5 (2.0, 3.0)</td>
<td>2.5 (2.0, 3.0)</td>
</tr>
</tbody>
</table>

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**Figure 1. Observed Concentration-Time Profiles of Pexidartinib and ZAAD-1006a from All Studies Including PK Simulations**

**Figure 2. Kinetograms of Pexidartinib and ZAAD-1006a from All Studies Including PK Simulations**

**Figure 3. Study State Exposure of Pexidartinib and ZAAD-1006a in Asian and Non-Asian Patients**

**Figure 4. Distribution of Pexidartinib and ZAAD-1006a from all Studies Including PK Simulations**