Larotrectinib is highly effective in children with TRK fusions (INV)

- Larotrectinib continues to demonstrate a favorable tolerability profile and histology-independent activity in pediatric patients harboring TRK fusions
- Recommended phase 2 dose in children: 100 mg/m² BID continuously, cap 100 mg/dose
  - No maximum tolerated dose reached
  - Similar exposure to adults at FDA
- Phase 2 portion of trial is enrolling globally
  - Infantile fibrosarcoma
  - Other CNS and extracranial TRK fusion solid cancers

Pediatric phase I trial design (SCOUT)*

- Objectives
  - Early evaluation of safety and tolerability
  - Early evaluation of pharmacokinetics
  - Early evaluation of efficacy and antitumor activity
  - Modified rolling 6 design* for Pediatric patients with TRK fusions: starting at 50 mg twice daily for ≥3 patients at each dose level during US evaluation
  - Continuous dose escalation: max 100 mg (n=9) then 162 mg total (n=24)
  - No maximum tolerated dose was defined

Patient and disease characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=24)</th>
<th>Non-TRK fusion (n=17)</th>
<th>TRK fusion (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>9 (4–21)</td>
<td>7 (4–21)</td>
<td>9 (4–21)</td>
</tr>
<tr>
<td>Sex</td>
<td>10 (42%)</td>
<td>8 (47%)</td>
<td>2 (29%)</td>
</tr>
<tr>
<td>Race</td>
<td>18 (75%)</td>
<td>12 (71%)</td>
<td>6 (86%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>13 (54%)</td>
<td>8 (47%)</td>
<td>5 (71%)</td>
</tr>
<tr>
<td>Extent of disease at study enrollment</td>
<td>4.5 (0.1–18.3)</td>
<td>4.4 (1–18.3)</td>
<td>4.7 (0.1–18.3)</td>
</tr>
<tr>
<td>Age group, n (%)</td>
<td>≥3 months – 21 years</td>
<td>8 (33)</td>
<td>6 (41)</td>
</tr>
<tr>
<td>No. of prior systemic therapies, n (%)</td>
<td>≥3</td>
<td>6 (25)</td>
<td>4 (57)</td>
</tr>
</tbody>
</table>

Adverse events related to larotrectinib* were generally low grade

- No lethal adverse events
- No discontinuations due to adverse events
- Common adverse events
  - Diarrhea – 11% – 11% 4% 4% – 8%
  - Hyperkalemia – 11% – 11% 4% 4% – 8%
  - Hypoalbuminemia – 11% – – – 11% 17% – – – 17%
  - Constipation – 22% – – – 22% 13% 4% – – 17%
  - Leukopenia – 22% – – – 22% 21% – – – 21%

Larotrectinib is highly effective in children with TRK fusions

- Objective response rate 85% (95% CI)
  - Complete response 58% (95% CI)
  - Fahler response 27% (95% CI)