**Larotrectinib**

Cat. No.: HY-12866  
CAS No.: 1223403-58-4  
Molecular Formula: C₂₁H₂₂F₂N₆O₂  
Molecular Weight: 428.44  
Target: Trk Receptor  
Pathway: Protein Tyrosine Kinase/RTK  
Storage: Powder  
-20°C  3 years  
4°C  2 years  
In solvent  
-80°C  6 months  
-20°C  1 month

**Solvent & Solubility**

In Vitro  
DMSO : ≥ 4.6 mg/mL (10.74 mM)  
* “≥” means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.3340 mL</td>
<td>11.6702 mL</td>
<td>23.3405 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4668 mL</td>
<td>2.3340 mL</td>
<td>4.6681 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2334 mL</td>
<td>1.1670 mL</td>
<td>2.3340 mL</td>
</tr>
</tbody>
</table>

Preparing Stock Solutions

Please refer to the solubility information to select the appropriate solvent.

**BIOLOGICAL ACTIVITY**

**Description**  
Larotrectinib (LOXO-101) is an ATP-competitive oral, selective inhibitor of the tropomyosin-related kinase (TRK) family receptors, with low nanomolar 50% inhibitory concentrations against all three isoforms (TRKA, B, and C).

**IC₅₀ & Target**

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>TrkA</th>
<th>TrkB</th>
<th>TrkC</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Vitro</td>
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</table>

Larotrectinib (LOXO-101) is an ATP-competitive oral inhibitor of the tropomyosin-related kinase (TRK) family of receptor kinases (TRKA, B, and C), with low nanomolar 50% inhibitory concentrations against all three isoforms, and 1,000-fold or greater selectivity relative to other kinases[1][2]. Measurement of proliferation following treatment with Larotrectinib (LOXO-101) demonstrates a dose-dependent inhibition of cell proliferation in all three cell lines. The IC₅₀ is less than 100 nM for CUTO-3.29 and less than 10 nM for KM12 and MO-91 consistent with the known potency of this drug for the TRK kinase family[3].

**In Vivo**

In rat and monkey studies, Larotrectinib (LOXO-101) demonstrates 33-100% oral bioavailability and 60-65% plasma...
protein binding. It has low brain penetration, and is well tolerated in 28 day (d) GLP toxicology studies. A single dose (30 mg/kg) of Larotrectinib (LOXO-101) reduces tyrosine phosphorylation of TRKA and downstream signal transduction (pERK) in the tumor >80%[1]. Athymic nude mice injected with KM12 cells are treated with Larotrectinib (LOXO-101) orally daily for 2 weeks. Dose-dependent tumor inhibition is observed demonstrating the ability of this selective compound to inhibit tumor growth in vivo[4]. Larotrectinib (LOXO-101) (200mg/kg/day p.o for six weeks) reduces leukemic infiltration to undetectable levels in the bone marrow and spleen compared to vehicle-treated mice. Mice treated with Larotrectinib (LOXO-101) are still alive and leukemia-free four weeks after the cessation of treatment, as determined by Xenogen imaging[5].

**PROTOCOL**

**Animal Administration [4]**

Athymic nude mice are used throughout the study. $5 \times 10^5$ KM12 cells are injected subcutaneously into the dorsal flank area of the mice. Tumor volume is monitored by direct measurement with calipers and calculated by the formula: length $\times$ (width$^2$)/2. Following the establishment of tumor and when the tumor size is between 150-200 mm$^2$, mice are randomly selected to receive diluent, 60 mg/kg/dose or 200 mg/kg/dose of Larotrectinib (LOXO-101). Larotrectinib (LOXO-101) is administered by oral gavage once daily for 14 days. After the last dose, tissue and blood are collected at 3, 6 and 24 hours post-treatment[4].

Mice are treated with Larotrectinib (LOXO-101) are still alive and leukemia-free four weeks after the cessation of treatment, as determined by Xenogen imaging[5].

**REFERENCES**


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Caution: Product has not been fully validated for medical applications. For research use only.

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