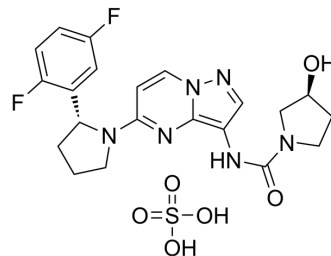


## Larotrectinib sulfate

<b>Cat. No.:</b>	HY-12866A
<b>CAS No.:</b>	1223405-08-0
<b>Molecular Formula:</b>	C <sub>21</sub> H <sub>24</sub> F <sub>2</sub> N <sub>6</sub> O <sub>6</sub> S
<b>Molecular Weight:</b>	526.51
<b>Target:</b>	Trk Receptor; Apoptosis
<b>Pathway:</b>	Neuronal Signaling; Protein Tyrosine Kinase/RTK; Apoptosis
<b>Storage:</b>	4°C, sealed storage, away from moisture * In solvent : -80°C, 1 year; -20°C, 6 months (sealed storage, away from moisture)



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : 50 mg/mL (94.96 mM; Need ultrasonic)  
H<sub>2</sub>O : 2 mg/mL (3.80 mM; ultrasonic and adjust pH to 2 with 1M HCl)

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	1.8993 mL	9.4965 mL	18.9930 mL
	5 mM	0.3799 mL	1.8993 mL	3.7986 mL
	10 mM	0.1899 mL	0.9496 mL	1.8993 mL

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

#### In Vivo

- Add each solvent one by one: PBS  
Solubility: 12.5 mg/mL (23.74 mM); Clear solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 3.25 mg/mL (6.17 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 3.25 mg/mL (6.17 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 3.25 mg/mL (6.17 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline  
Solubility: ≥ 2.5 mg/mL (4.75 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.5 mg/mL (4.75 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

Larotrectinib sulfate (LOXO-101 sulfate; ARRY-470 sulfate) 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).		
<b>IC<sub>50</sub> &amp; Target</b>	TrkA	TrkB	TrkC
<b>In Vitro</b>	<p>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<sup>[1][2]</sup>. Measurement of proliferation following treatment with Larotrectinib (LOXO-101) demonstrates a dose-dependent inhibition of cell proliferation in all three cell lines. The IC<sub>50</sub> 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<sup>[3]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>		
<b>In Vivo</b>	<p>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 &gt;80%<sup>[1]</sup>. Athymic nude mice injected with KM12 cells are treated with Larotrectinib sulfate orally daily for 2 weeks. Dose-dependent tumor inhibition is observed demonstrating the ability of this selective compound to inhibit tumor growth in vivo<sup>[4]</sup>. 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 sulfate are still alive and leukemia-free four weeks after the cessation of treatment, as determined by Xenogen imaging<sup>[5]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>		

## PROTOCOL

### Animal Administration<sup>[4]</sup>

Mice<sup>[4]</sup>

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:  $\text{length} \times (\text{width}^2)/2$ . Following the establishment of tumor and when the tumor size is between 150-200 mm<sup>2</sup>, 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<sup>[4]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Cell Rep Med. 2023 Jan 10;100911.
- Eur J Med Chem. 2020 Aug 30;207:112744.
- Mol Oncol. 2022 Oct 1.
- Mol Cancer Ther. 2021 Oct 8;molcanther.MCT-21-0632-A.2021.
- Spectrochim Acta A Mol Biomol Spectrosc. 2023 Nov 5, 300, 122914.

See more customer validations on [www.MedChemExpress.com](http://www.MedChemExpress.com)

## REFERENCES

[1]. Doebele RC, et al. An Oncogenic NTRK Fusion in a Patient with Soft-Tissue Sarcoma with Response to the Tropomyosin-Related Kinase Inhibitor LOXO-101. Cancer

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Discov. 2015 Oct;5(10):1049-57.

[2]. Karyn Bouhana, et al. LOXO-101, a pan TRK inhibitor, For The Treatment Of TRK-driven Cancers.

[3]. Nagasubramanian R, et al. Infantile Fibrosarcoma With NTRK3-ETV6 Fusion Successfully Treated With the Tropomyosin-Related Kinase Inhibitor LOXO-101. *Pediatr Blood Cancer*. 2016 Aug;63(8):1468-70.

[4]. Kathryn G, et al. Genetic Modeling and Therapeutic Targeting of ETV6-NTRK3 with Loxo-101 in Acute Lymphoblastic Leukemia. *Blood* 2016 128:278.

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

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