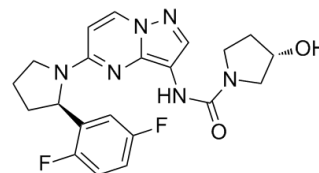


Data Sheet

Product Name:	LOXO-101
Cat. No.:	HY-12866
CAS No.:	1223403-58-4
Molecular Formula:	C ₂₁ H ₂₂ F ₂ N ₆ O ₂
Molecular Weight:	428.44
Target:	Trk Receptor
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO: ≥ 4.6 mg/mL



BIOLOGICAL ACTIVITY:

LOXO-101 is a potent, ATP competitive TRK inhibitor with IC₅₀s in low nanomolar range for inhibition of all TRK family members in binding and cellular assays, with 100x selectivity over other kinases, with 2 to 20 nM cellular potency against the TRKA, TRKB, and TRKC kinases.

In vivo: A single dose (30 mg/kg) of LOXO-101 reduced tyrosine phosphorylation of TRKA and downstream signal transduction (pERK) in the tumor >80%. LOXO-101 was well tolerated up to 200 mg/kg/day for 14 d in this model.

In vitro: LOXO-101 was evaluated for off-target kinase enzyme inhibition against a panel of 226 non-TRK kinases at a compound concentration of 1,000 nM and ATP concentrations near the K_m for each enzyme. LOXO-101 demonstrated greater than 50% inhibition for only one non-TRK kinase (TNK2 IC₅₀ = 576 nM).

References:

- [1]. 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.
- [2]. LOXO-101, a pan TRK inhibitor, For The Treatment Of TRK-driven Cancers. Lori Kunkel et al.
- [3]. Robert C. Doebele et al. An oncogenic NTRK fusion in a soft tissue sarcoma patient with response to the tropomyosin-related kinase (TRK) inhibitor LOXO-101. *Cancer Discov*. 2015 Oct; 5(10): 1049-1057.

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

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