Repotrectinib

Cat. No.: HY-103022

CAS No.: 1802220-02-5

Molecular Formula: $C_{18}H_{18}FN_5O_2$

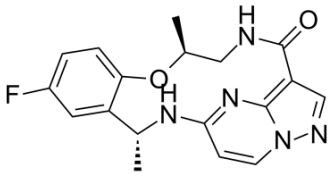
Molecular Weight: 355.37

Target: ROS; Trk Receptor; ALK

Pathway: Protein Tyrosine Kinase/RTK; Neuronal Signaling

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 : ≥ 83.3 mg/mL (234.40 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8140 mL	14.0698 mL	28.1397 mL
5 mM	0.5628 mL	2.8140 mL	5.6279 mL
10 mM	0.2814 mL	1.4070 mL	2.8140 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.03 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.03 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Repotrectinib (TPX-0005) is a potent ROS1 (IC_{50}=0.07 nM) and TRK (IC_{50}=0.83/0.05/0.1 nM for TRKA/B/C) inhibitor. Repotrectinib potently inhibits WT ALK (IC_{50}=1.01 nM). Repotrectinib has anti-cancer activity[1][2].

IC_{50} & Target

IC50: 0.07 nM (ROS1), 0.83/0.05/0.1 nM (TRKA/B/C), 1.01 nM (ALK), 1.04 nM (JAK2), 1.66 nM (LYN), 5.3 nM (Src), 6.96 nM (FAK) [1][2]

In Vitro

Repotrectinib (TPX-0005) inhibits mutant ALKs including ALK G1202R (IC_{50}=1.26 nM) and ALK L1196M (IC_{50}=1.08 nM). Repotrectinib also inhibits a variety of other kinases, including JAK2, LYN, Src, and FAK (IC_{50}=1.04, 1.66, 5.3, and 6.96 nM, respectively)[1].

	Repotrectinib effectively overcomes this primary resistance (IC_{50}=100 nM in cell proliferation assay) with strong inhibition of the phosphorylation of EML4-ALK (IC_{50}=13 nM) and the SRC substrate paxillin (IC_{50}=107 nM). Repotrectinib inhibits H2228 cell migration in a wound healing assay with similar activity to saracatinib[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Repotrectinib (TPX-0005) effectively inhibits tumor growth in vivo in ALK WT and ALK G1202R xenografts[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Dayong Zhai, et al. Abstract 2132: The novel, rationally-designed, ALK/SRC inhibitor TPX-0005 overcomes multiple acquired resistance mechanisms to current ALK inhibitors. Cancer Research. July 2016

[2]. Karachaliou N, et al. Common Co-activation of AXL and CDCP1 in EGFR-mutation-positive Non-smallcell Lung Cancer Associated With Poor Prognosis. EBioMedicine. 2018 Mar;29:112-127.

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