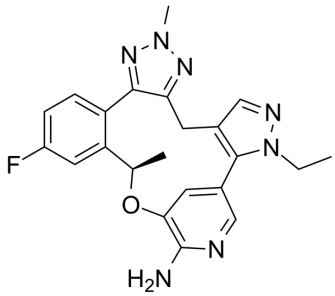
Zidesamtinib

Cat. No.:	HY-152292
CAS No.:	2739829-00-4
Molecular Formula:	$C_{22}H_{22}FN_7O$
Molecular Weight:	419.45
Target:	ROS Kinase
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 : 50 mg/mL (119.20 mM; ultrasonic and warming and heat to 65°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3841 mL	11.9204 mL	23.8407 mL
	5 mM	0.4768 mL	2.3841 mL	4.7681 mL
	10 mM	0.2384 mL	1.1920 mL	2.3841 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: ≥ 1.25 mg/mL (2.98 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (2.98 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.98 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Zidesamtinib (NVL-520) is a potent, selective, orally active and brain-penetrant inhibitor of diverse ROS1 fusions and resistance mutations, with IC_{50}s of 0.7 and 7.9 nM for wild-type ROS1 and ROS1 G2032R, respectively, and spares TRK inhibition. Zidesamtinib can be used for the research of cancer[1].

In Vitro

Zidesamtinib (72 h) inhibits the growth of seven cell lines expressing wild-type ROS1 fusions, with average IC_{50}s of 0.4 nM[1]. Zidesamtinib (72 h) inhibits the growth of six cell lines harboring ROS1 fusions with the G2032R mutation, with average IC_{50}s of 1.6 nM[1].

	Zidesamtinib (72 h) potently inhibits the non-G2032R ROS1 mutants, with IC_{50}s ≤ 1.5 nM[1]. Zidesamtinib (10-1000 nM; 4 weeks) suppresses colony formation in NIH3T3 cells expressing wild-type ROS1 fusions and expressing ROS1 fusions with G2032R[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Zidesamtinib (0.04-15 mg/kg; p.o. twice daily for 28 d) induces tumor regression at all doses ≥0.2 mg/kg in wild-type ROS1 xenograft models[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female athymic Nude-Foxn1^{nu} mice were implanted subcutaneously with tumor fragments from model CTG-0848[1]
Dosage:	0.04, 0.2, 1, 5, 15 mg/kg
Administration:	Oral gavage twice daily for 21 days
Result:	Inhibited the tumor volumes.

REFERENCES

[1]. Drilon A, et, al. NVL-520 is a selective, TRK-sparing, and brain-penetrant inhibitor of ROS1 fusions and secondary resistance mutations. Cancer Discov. 2022 Dec 13;CD-22-0968.

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