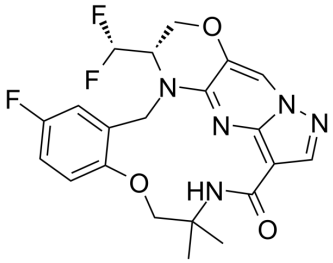
TPX-0131

Cat. No.:	HY-139279
CAS No.:	2648641-36-3
Molecular Formula:	$C_{21}H_{20}F_3N_5O_3$
Molecular Weight:	447.41
Target:	ALK
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 : 25 mg/mL (55.88 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2351 mL	11.1754 mL	22.3509 mL
	5 mM	0.4470 mL	2.2351 mL	4.4702 mL
	10 mM	0.2235 mL	1.1175 mL	2.2351 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: ≥ 2.08 mg/mL (4.65 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.65 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.65 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TPX-0131 is a potent, selective, CNS-penetrant and orally active inhibitor of wild-type ALK (IC_{50} of 1.4 nM) and ALK-resistant mutation, e.g. G1202R (IC_{50} of 0.3 nM), L1196M (IC_{50} of 0.3 nM). TPX-0131 has strong antitumor activities[1].

IC_{50} & Target

IC50: 1.4 nM (Wild-typr AKT); 0.2-6.6 nM (mutant ALK variants)[1]

In Vitro

TPX-0131 potently inhibits wild-type ALK (IC_{50} = 1.4 nM) and 26 ALK resistance mutations. TPX-0131 inhibits C1156Y, E1210K/S1206C, L1198F/C1156Y, L1196M/L1198F, E1210K, L1196M, T1151M, deleted G1202, S1206R, G1202R/L1198F,

F1174L, F1245C, R1275Q, and G1202R ALK mutations with IC50 values of <1 nM. TPX0131 has IC_{50} values of 1-2 nM for the following ALK mutations: L1198F, L1152R, F1174S, T1151-L1152 insT, V1180L, G1269A, F1174C. TPX-0131 is less active against ALK mutations including I1171N, L1152P, D1203N, D1203N/E1210K, and G1269S, with IC_{50} values of 2-7 nM[1].
TPX-0131 is a potent inhibitor of ALK autophosphorylation in Ba/F3 cells expressing EML4-ALK G1202R solvent front, EML4-ALK G1202R/L1196M, or EML4-ALK G1202R/L1198F mutations, with IC50 values of approximately 3-10 nM[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

TPX-0131 (2-10 mg/kg; p.o.; twice a day; for 2 weeks) treatment at 2 mg/kg, 5 mg/kg, and 10 mg/kg resulted in dose-dependent tumor growth inhibition (TGI) of 64%, 120%, and 200% (complete regression), respectively[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female SCID/beige mice (5-8 weeks old) bearing Ba/F3 cells[1]
Dosage:	2 mg/kg, 5 mg/kg, and 10 mg/kg
Administration:	p.o.; twice a day; for 2 weeks
Result:	Caused complete tumor regression in ALK mutation-dependent xenograft models.

REFERENCES

[1]. Brion W Murray, et al. TPX-0131, a Potent CNS-Penetrant, Next-Generation Inhibitor of Wild-Type ALK and ALK-Resistant Mutations. Mol Cancer Ther. 2021 Jun 22;molcanther.0221.2021.

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