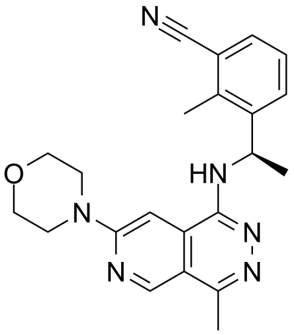
MRTX0902

Cat. No.:	HY-145926
CAS No.:	2654743-22-1
Molecular Formula:	$C_{22}H_{24}N_6O$
Molecular Weight:	388.47
Target:	Ras
Pathway:	GPCR/G Protein
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 : 12.5 mg/mL (32.18 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5742 mL	12.8710 mL	25.7420 mL
	5 mM	0.5148 mL	2.5742 mL	5.1484 mL
	10 mM	0.2574 mL	1.2871 mL	2.5742 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (3.22 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MRTX0902 is an orally active and potent SOS1 inhibitor with an IC_{50} of 46 nM (WO2021127429A1; Example 12-10)[1].

IC_{50} & Target

KRAS-SOS1
46 nM (IC_{50})

In Vitro

MRTX0902 (compound 32) (1 μM; 0, 2, 4, 8, 15, and 30 minutes) shows a moderate Cl_{int} value of 195 mL/min/kg in human liver microsome and a low lipophilicity with cLogP of 3.4[1].
MRTX0902 displays high selectivity on SOS1 (K_i=2 nM) over SOS2 and EGFR (both K_i values >10,000 nM), MRTX0902 inhibits MKN1 cells with an IC_{50} value of 29 nM[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

MRTX0902 (compound 32) (25, 50 mg/kg; p.o.; twice daily; 25 d) shows anti-tumor effect in mouse model and results tumor

regression[1].
MRTX0902 (1-3 mg/kg for i.v. or 10-30 mg/kg for p.o.; single dose) exhibits good brain penetrance, low clearance, and high bioavailability[1].
PK Parameters for MRTX0902 across Species[1]

Parameter	Route	Dose (mg/kg)	Cl (mL/min/kg)	$V_{d,ss}$ (L/kg)	$T_{1/2}$(iv) (h)	F (%)
Mouse	IV/PO	3/30	4.4	0.28	1.3	69
Rat	IV/PO	1/10	14.6	0.28	0.62	83
Dog	IV/PO	2/10	7.6	0.48	0.86	38

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

Animal Model:	Female CD-1 mice[1]
Dosage:	50 mg/kg
Administration:	Oral gavage; twice daily; 1 day
Result:	Resulted free drug exposure in the brain as well as the efflux ratio in the Caco-2 assay (ER = 1.5). Showed short half-life of the compound in mice ($T_{1/2}$ = 1.3 h).

Animal Model:	MIA PaCa-2 xenograft model in mouse[1]
Dosage:	25 mg/kg; 50 mg/kg
Administration:	Oral gavage; twice daily; 25 days
Result:	Reduced tumor growth by 41% and 53% at 25 mg/kg and 50 mg/kg administration.

REFERENCES

[1]. Ketcham JM, et al. Design and Discovery of MRTX0902, a Potent, Selective, Brain-Penetrant, and Orally Bioavailable Inhibitor of the SOS1:KRAS Protein-Protein Interaction. J Med Chem. 2022 Jul 28;65(14):9678-9690.

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