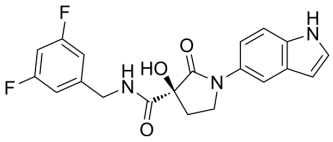
M8891

Cat. No.:	HY-133016
CAS No.:	1464842-09-8
Molecular Formula:	$C_{20}H_{17}F_2N_3O_3$
Molecular Weight:	385.36
Target:	MetAP
Pathway:	Metabolic Enzyme/Protease
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 90 mg/mL (233.55 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5950 mL	12.9749 mL	25.9498 mL
	5 mM	0.5190 mL	2.5950 mL	5.1900 mL
	10 mM	0.2595 mL	1.2975 mL	2.5950 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 (5.40 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.40 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.40 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

M8891 is an orally active, reversible and brain penetrant Methionine Aminopeptidase-2 (MetAP-2) inhibitor with an IC_{50} of 54 nM and a K_i of 4.33 nM. M8891 does not inhibit MetAP-1 (IC_{50}>10 μM)[1]. M8891 inhibits growth of primary endothelial cells as well as tumor cells and demonstrates antiangiogenic and antitumoral activity[2].

IC_{50} & Target

IC50: 54 nM (MetAP-2)[1]
Ki: 4.33 nM (MetAP-2)[1]

In Vitro

M8891 has an IC_{50} of 20 nM for HUVEC proliferation[1].

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

In Vivo

M8891 (po; 20 mg/kg; once a day for 14 days) exhibits strong tumor growth inhibition[1].
M8891 (iv; 0.2 mg/kg) shows low clearance (CL ~0.03-0.4 L/h/kg corresponding to ~1-6% of the liver blood-flow), small to medium volume of distribution (Vss ~0.23-1.3 L/kg), and medium to high oral bioavailability (F ~40-80%)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female CD-1 nude mice aged 6-7 weeks with human U87-MG glioblastoma[1]
Dosage:	20 mg/kg
Administration:	Po; once a day for 14 days
Result:	Exhibited strong tumor growth inhibition.

Animal Model:	Rat, dog and monkey[1]
Dosage:	0.2 mg/kg (Pharmacokinetic Analysis)
Administration:	IV
Result:	Showed low clearance (CL ~0.03-0.4 L/h/kg corresponding to ~1-6% of the liver blood-flow), small to medium volume of distribution (Vss ~0.23-1.3 L/kg), and medium to high oral bioavailability (F ~40-80%).

REFERENCES

[1]. Heinrich T, et al. Identification of Methionine Aminopeptidase-2 (MetAP-2) Inhibitor M8891: A Clinical Compound for the Treatment of Cancer. J Med Chem. 2019 Dec 26;62(24):11119-11134.

[2]. Manja Friese-Hamim, et al. Abstract 3075: Antitumor activity of M8891, a potent and reversible inhibitor of methionine aminopeptidase 2.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA