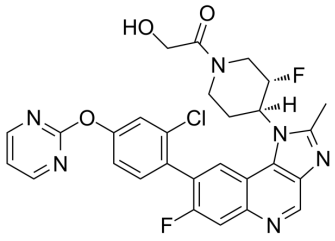
MAP855

Cat. No.:	HY-145702
CAS No.:	1660107-77-6
Molecular Formula:	$C_{28}H_{23}ClF_2N_6O_3$
Molecular Weight:	564.97
Target:	MEK; ERK
Pathway:	MAPK/ERK Pathway; Stem Cell/Wnt
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 : 100 mg/mL (177.00 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7700 mL	8.8500 mL	17.7001 mL
	5 mM	0.3540 mL	1.7700 mL	3.5400 mL
	10 mM	0.1770 mL	0.8850 mL	1.7700 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 (4.43 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.43 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MAP855 is a highly potent, selective, ATP-competitive and orally active MEK1/2 kinase inhibitor (MEK1 ERK2 cascade IC_{50}=3 nM, pERK EC_{50}=5 nM). MAP855 shows equipotent inhibition of wild-type and mutant MEK1/2[1].

IC_{50} & Target

ERK	MEK1
5 nM (EC50)	3 nM (IC_{50})

In Vitro

MAP855 (compound 30) has single-digit nM inhibition of pERK and proliferation in A375 cells (pERK EC_{50}=5 nM)[1].

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

Cell Proliferation Assay

Cell Line:	A375 cells[1]
Concentration:	0-10 nM
Incubation Time:	72 hours
Result:	Showed single-digit nM inhibition of pERK and proliferation in A375 cells (pERK EC_{50}=5 nM).

In Vivo

MAP855 (3 mg/kg for i.v., 10 mg/kg for p.o.; single) has good oral bioavailability and medium clearance in rodents[1].
MAP855 (30 mg/kg; p.o., b.i.d, 14 days) achieves comparable efficacy to trametinib dosed at the mouse MTD without any body weight loss[1].
Pharmacokinetic Parameters of MAP855 in mouse, rat and dog[1].

	mouse	rat	dog
CL [mL/min*kg]	32	35	22
V_{ss} [l/kg]	2.6	2.0	1.8
AUC po d.n. [μM*h]	0.4	0.6	1.4
Oral BAV [% F]	44	65	100

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

Animal Model:	Male Wistar Rats[1]
Dosage:	3 mg/kg for i.v., 10 mg/kg for p.o.
Administration:	i.v. and p.o., single
Result:	Showed good oral bioavailability and medium clearance.

Animal Model:	A375 Tumor Bearing Mice[1]
Dosage:	30 mg/kg
Administration:	p.o., b.i.d, 14 days
Result:	Achieved comparable efficacy to trametinib dosed at the mouse MTD without any body weight loss.

REFERENCES

[1]. Poddutoori R, et al. Discovery of MAP855, an Efficacious and Selective MEK1/2 Inhibitor with an ATP-Competitive Mode of Action. J Med Chem. 2022;65(5):4350-4366.

Caution: Product has not been fully validated for medical applications. For research use only.

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