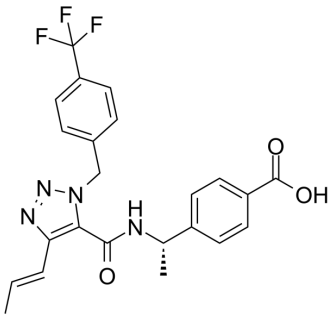
EP4 receptor antagonist 1

Cat. No.:	HY-133123
CAS No.:	2287259-07-6
Molecular Formula:	$C_{23}H_{21}F_3N_4O_3$
Molecular Weight:	458.43
Target:	Prostaglandin Receptor
Pathway:	GPCR/G Protein
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (218.14 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1814 mL	10.9068 mL	21.8136 mL
	5 mM	0.4363 mL	2.1814 mL	4.3627 mL
	10 mM	0.2181 mL	1.0907 mL	2.1814 mL

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

BIOLOGICAL ACTIVITY

Description

EP4 receptor antagonist 1 is a highly potent and selective competitive prostanoid EP4 receptor antagonist for cancer immunotherapy. EP4 receptor antagonist 1 inhibits human and mouse EP4 receptor with IC_{50}s of 6.1 nM and 16.2 nM, respectively. IC_{50}s >10 μM for human EP1, EP2,and EP3 receptors[1].

IC_{50} & Target

IC50: 6.1 nM (human EP4 receptor), 16.2 nM (mouse EP4 receptor)[1]

In Vitro

The antagonistic effect of EP4 receptor antagonist 1 (Compounds 59) on human EP4 in calcium flux assay with an IC_{50} of 6.1±0.2 nM in CHO-$G_{\alpha 16}$ cells overexpressing human EP4 receptor. The antagonistic effect of EP4 receptor antagonist 1 on human EP4 in calcium flux assay with an IC_{50} of 16.2±1.7 nM in CHO-$G_{\alpha 16}$ cells overexpressing mouse EP4 receptor[1].

EP4 receptor antagonist 1 dose dependently inhibits PGE2-stimulated cAMP accumulation in HEK293-EP4 cells with an IC_{50} of 18.7±0.6 nM. EP4 receptor antagonist 1 dose-dependently inhibits the activity of the CRE reporter in HEK293 cells with an IC_{50} of 5.2±0.4 nM.EP4 receptor antagonist 1 dose-dependently inhibits PGE2-stimulated β-arrestin recruitment in HEK293-EP4 cells with an IC_{50} of 0.4±0.1 nM[1].

EP4 receptor antagonist 1 (1 nM-10 μM) reverses PGE2-induced ERK phosphorylation in a concentration-dependent manner [1].

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

Western Blot Analysis[1]

Cell Line:	CHO-EP4 cells
Concentration:	1 nM, 100 nM, 10 μM
Incubation Time:	Pretreated for 20 min and then subjected to 30 nM PGE2 simulation for 10 min.
Result:	Reversed PGE2-induced ERK phosphorylation in a concentration-dependent manner.

In Vivo

EP4 receptor antagonist 1 (16, 50, and 150 mg/kg; orally; once daily for two weeks) causes significant inhibition of tumor growth in BALB/c female mice. No significant body weight loss is found in any mouse cohorts. EP4 receptor antagonist 1 is well tolerated in mice at the tested dosage[1].

EP4 receptor antagonist 1 (1 mg/kg; intravenously) demonstrates moderate clearance (CL=1.7 L/h/kg) in mice with a corresponding favorable half-life ($t_{1/2}$) of 4.1 h. EP4 receptor antagonist 1 (5 mg/kg; orally) exhibits good bioavailability (F=48.0%) in mice with a corresponding favorable half-life ($t_{1/2}$) of 4.7 h[1].

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

Animal Model:	BALB/c female mice (6-week-old)bearing CT26 colon cancer model[1]
Dosage:	16, 50, and 150 mg/kg
Administration:	Orally; once daily for two weeks
Result:	Tumor growth inhibition (TGI) was 24.6% at 16 mg/ kg, 54.7% at 50 mg/kg, and 63.8% at 150 mg/kg.

Animal Model:	BALB/c female mice[1]
Dosage:	1 mg/kg and 5 mg/kg (Pharmacokinetic Analysis)
Administration:	Intravenously or orally at a dose of 1 mg/kg (5 mL/kg) and 5 mg/kg (10 mL/kg),respectively.
Result:	Demonstrated moderate clearance (CL=1.7 L/h/kg) in mice with a corresponding favorable half-life ($t_{1/2}$) of 4.1 h at a dose of 1 mg/kg (intravenously). Exhibited good bioavailability (F=48.0%) in mice with a corresponding favorable half-life ($t_{1/2}$) of 4.7 h at a dose of 5 mg/kg (orally).

REFERENCES

[1]. Yang JJ, et al. Discovery and Characterization of 1H-1,2,3-Triazole Derivatives as Novel Prostanoid EP4 Receptor Antagonists for Cancer Immunotherapy. J Med Chem. 2020 Jan 23;63(2):569-590.

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

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