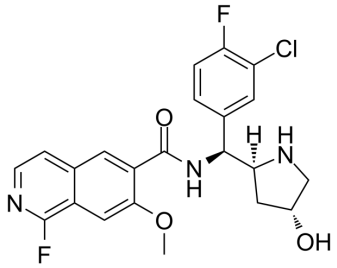
DS89002333

Cat. No.:	HY-150072
CAS No.:	2832159-79-0
Molecular Formula:	$C_{22}H_{20}ClF_2N_3O_3$
Molecular Weight:	447.86
Target:	PKA
Pathway:	Stem Cell/Wnt
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (223.28 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2328 mL	11.1642 mL	22.3284 mL
	5 mM	0.4466 mL	2.2328 mL	4.4657 mL
	10 mM	0.2233 mL	1.1164 mL	2.2328 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 (5.58 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.58 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.58 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

DS89002333 is an orally active and potent PRKACA inhibitor, with an IC_{50} of 0.3 nM. DS89002333 shows good anti-tumor activity in an FL-HCC patient-derived xenograft model (expressing the DNAJB1-PRKACA fusion gene). DS89002333 can be used in study of fibrolamellar hepatocellular carcinoma (FL-HCC)[1].

IC_{50} & Target

PRKACA
0.3 nM (IC_{50})

In Vitro

DS89002333 (0.001, 0.01, 0.1, 1, 10 μM; 30 min) inhibits phosphorylation of CREB in a dose-dependent manner in NIH/3T3

cells (phosphorylation status of CREB as a marker of intracellular PRAKACA inhibitory activity)[1].

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

Cell Viability Assay[1]

Cell Line:	NIH/3T3 cells
Concentration:	0.001, 0.01, 0.1, 1, 10 μM
Incubation Time:	30 min
Result:	Showed a dose-dependent decrease in phosphorylation of CREB, with an IC_{50} of 50 nM.

In Vivo

DS89002333 (12.5, 50 mg/kg; p.o.; twice daliy for 5 days) shows anti-tumor activity in an NIH/3T3-fusion allograft model[1].

DS89002333 (3, 30 mg/kg; p.o.; twice daliy for 22 days) shows significant anti-tumor activity in FL-HCC PDX xenograft model [1].

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

Animal Model:	Female nude mice (NIH/3T3-fusion allograft model)[1].
Dosage:	12.5, 50 mg/kg
Administration:	Oral administration, twice daliy for 5 days.
Result:	Exhibited anti-tumor activity without body weight loss.

Animal Model:	Female NOD SCID mice (FL-HCC PDX xenograft model)[1].
Dosage:	3, 30 mg/kg
Administration:	Oral administration, twice daliy for 22 days.
Result:	Significant inhibited tumor in mice, and showed temporary body weight loss (at 30 mg/kg), but this resolved following continuous dosing.

REFERENCES

[1]. Toyota A, et al. ovel protein kinase cAMP-Activated Catalytic Subunit Alpha (PRKACA) inhibitor shows anti-tumor activity in a fibrolamellar hepatocellular carcinoma model. Biochem Biophys Res Commun. 2022 Sep 17;621:157-161.

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