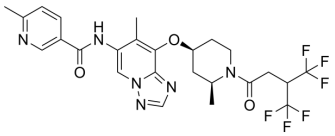
RORγt Inverse agonist 10

Cat. No.:	HY-133552
CAS No.:	2413986-35-1
Molecular Formula:	$C_{25}H_{26}F_6N_6O_3$
Molecular Weight:	572.5
Target:	ROR
Pathway:	Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor
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 (174.67 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7467 mL	8.7336 mL	17.4672 mL
	5 mM	0.3493 mL	1.7467 mL	3.4934 mL
	10 mM	0.1747 mL	0.8734 mL	1.7467 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: ≥ 10 mg/mL (17.47 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 10 mg/mL (17.47 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 10 mg/mL (17.47 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

RORγt Inverse agonist 10 is a potent and orally bioavailable RORγt (retinoic acid receptor-related orphan nuclear receptor gamma t) inverse agonist, with an IC_{50} of 51 nM. RORγt is a major transcription factor of genes related to psoriasis pathogenesis such as IL-17A, IL-22, and IL-23R[1]

IC_{50} & Target

RORγt
51 nM (IC_{50})

In Vitro

RORγt Inverse agonist 10 has a good liver microsome stability (human CL_{int}=0.010 mL/min/mg, mouse CL_{int}=0.030 mL/min/mg)[1].

RORγt Inverse agonist 10 suppresses the IL-17A production in a dose-dependent manner with an IC_{50} of 130 nM in a human whole-blood assay[1].

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

In Vivo

RORγt Inverse agonist 10 (3-100 mg/kg; p.o.) shows robust and dose-dependent inhibitory effect on the IL-17A production in mouse IL-18/23-induced cytokine expression model[1].

RORγt Inverse agonist 10 (1.145 mg/kg; p.o.) shows a high AUC of 15000 nM*h and $t_{1/2}$ of 3.6 hours[1].

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

Animal Model:	C57/BL6 male mice, mouse IL-18/23-induced cytokine expression model[1]
Dosage:	3 mg/kg, 10 mg/kg, 30 mg/kg, 100 mg/kg
Administration:	Oral administration
Result:	Significantly inhibited the IL-17A production in a dose-dependent manner.

Animal Model:	Mice[1]
Dosage:	1.145 mg/kg (Pharmacokinetic Analysis)
Administration:	Oral administration
Result:	AUC=15000 nM*h, $t_{1/2}$=3.6 hours.

REFERENCES

[1]. Ryota Nakajima, et al. Discovery of [1,2,4]Triazolo[1,5- a]pyridine Derivatives as Potent and Orally Bioavailable RORγt Inverse Agonists. ACS Med Chem Lett. 2020 Feb 27;11(4):528-534.

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