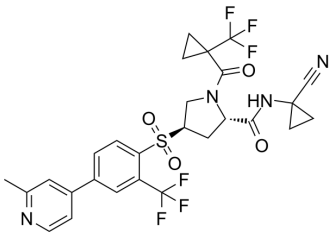
RO5461111

Cat. No.:	HY-114374
CAS No.:	1252637-46-9
Molecular Formula:	$C_{27}H_{24}F_6N_4O_4S$
Molecular Weight:	614.56
Target:	Cathepsin
Pathway:	Metabolic Enzyme/Protease
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 (162.72 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6272 mL	8.1359 mL	16.2718 mL
	5 mM	0.3254 mL	1.6272 mL	3.2544 mL
	10 mM	0.1627 mL	0.8136 mL	1.6272 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: ≥ 1.67 mg/mL (2.72 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (2.72 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

RO5461111 a highly specific and orally active antagonist of Cathepsin S with IC_{50}s of 0.4 nM (human Cathepsin S) and 0.5 nM (murine Cathepsin S), respectively. RO5461111 can effectively inhibit the activation of antigen-specific T cells and B cells. RO5461111 can improve pulmonary inflammation and lupus nephritis[1][2].

IC_{50} & Target	
human Cathepsin S 0.4 nM (IC_{50})	murine Cathepsin S 0.5 nM (IC_{50})

In Vitro

RO5461111 (16 h) □ □ (RAJI) □□ (A20) □□ CD4 T □□□□ CD4/CD8 □□□□ T □□□□□□□□□ □[1]□

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

In Vivo

RO5461111 (0.1-100 mg/kg; p.o.; single dose) suppresses T cell priming and antisheep IgG upon vaccination with sheep IgG in BALB/c mice[1].

RO5461111 (1.31 mg/mouse or 30 mg/kg; p.o.; 8 weeks) disrupts germinal centres (as CXCL12) and reduces hypergammaglobulinemia and lupus autoantibody production F in MRL-Fas(lpr) mice. And RO5461111 reduces lung inflammation and improves lupus nephritis[1].

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

Animal Model:	Female MRL-Fas(lpr) mice (12-week-old; with proteinuria/serum creatinine levels up)[1]
Dosage:	262.5 mg/kg chow; or 5 mg/mouse with 1.31 mg/mouse
Administration:	Oral gavage; 8 weeks
Result:	Reduced the activation and expansion of spleen dendritic cells, CD4, double-negative T cells and plasma cells. Reduced plasma levels of IL-10 and TNF-α.

REFERENCES

[1]. Sanchez RA, et al. Preparation of proline dipeptidyl nitrile derivatives as cathepsin, particularly cathepsin S and L, inhibitors: United States, US20100267722. 2010-10-21.

[2]. Rupanagudi KV, et al. Cathepsin S inhibition suppresses systemic lupus erythematosus and lupus nephritis because cathepsin S is essential for MHC class II-mediated CD4 T cell and B cell priming. Ann Rheum Dis. 2015 Feb;74(2):452-63.

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