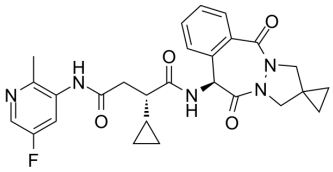
SPL-707

Cat. No.:	HY-111360
CAS No.:	2195361-33-0
Molecular Formula:	$C_{27}H_{28}FN_5O_4$
Molecular Weight:	505.54
Target:	γ-secretase
Pathway:	Neuronal Signaling; 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 (197.81 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9781 mL	9.8904 mL	19.7808 mL
	5 mM	0.3956 mL	1.9781 mL	3.9562 mL
	10 mM	0.1978 mL	0.9890 mL	1.9781 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: ≥ 5 mg/mL (9.89 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (9.89 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SPL-707 is an orally active, selective signal peptide peptidase-like 2a (SPPL2a) inhibitor with an IC_{50} of 77 nM for hSPPL2a. SPL-707 inhibits γ-secretase (IC_{50}=6.1 μM) and SPP (IC_{50}=3.7 μM). SPL-707 has the potential for autoimmune diseases research by targeting B cells and dendritic cells[1].

IC_{50} & Target

IC50: 77 nM (SPPL2a), 6.1 μM (γ-secretase) and 3.7 μM (SPP)[1]

In Vitro

SPL-707 (Compound 40) inhibits mouse SPPL2a (IC_{50}=0.18 μM), rat SPPL2a (IC_{50}=0.056 μM) and human SPPL2a (IC_{50}=0.16 μM), human SPPL2b (IC_{50}=0.43 μM) by a high content imaging assay (HCA)[1].

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

In Vivo

SPL-707 (Compound 40; 3-30 mg/kg; orally; b.i.d.; for 11 days) leads to a reduction in B cells and myeloid dendritic cells without affecting γ-secretase activity[1].

SPL-707 (3 mg/kg of po and 1 mg/kg of iv) has a CL of 6 mL/min•kg, and an AUC of 8787 h•nM[1].

SPL-707 (1, 3 mg/kg; b.i.d.; first dose at 0 h, second dose at 8 h) achieves full inhibition of CD74/p8 processing in spleen in female Lewis rats[1].

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

Animal Model:	Mice with 5-12 weeks of age[1]
Dosage:	3, 10, and 30 mg/kg
Administration:	Orally; b.i.d. (with 8 and 16 h dosing intervals); for 11 days
Result:	Led to a reduction in B cells and myeloid dendritic cells without affecting γ-secretase activity.

Animal Model:	Female Sprague−Dawley rat[1]
Dosage:	3 mg/kg of po and 1 mg/kg of iv (Pharmacokinetic Analysis)
Administration:	PO or IV
Result:	Had a CL of 6 mL/min•kg, and an AUC of 8787 h•nM.

REFERENCES

[1]. Velcicky J, et al. Discovery of the First Potent, Selective, and Orally Bioavailable Signal Peptide Peptidase-Like 2a (SPPL2a) Inhibitor Displaying Pronounced Immunomodulatory Effects In Vivo. J Med Chem. 2018 Feb 8;61(3):865-880.

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