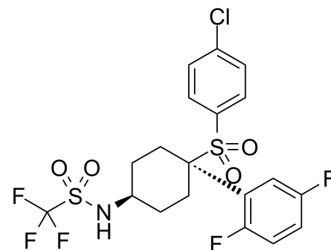


## MRK-560

<b>Cat. No.:</b>	HY-14174		
<b>CAS No.:</b>	677772-84-8		
<b>Molecular Formula:</b>	C <sub>19</sub> H <sub>17</sub> ClF <sub>5</sub> NO <sub>4</sub> S <sub>2</sub>		
<b>Molecular Weight:</b>	517.92		
<b>Target:</b>	γ-secretase		
<b>Pathway:</b>	Neuronal Signaling; Stem Cell/Wnt		
<b>Storage:</b>	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 (193.08 mM; Need ultrasonic)

Concentration	Solvent	Mass	1 mg	5 mg	10 mg
			1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM		1.9308 mL	9.6540 mL	19.3080 mL
	5 mM		0.3862 mL	1.9308 mL	3.8616 mL
	10 mM		0.1931 mL	0.9654 mL	1.9308 mL

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

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 2.5 mg/mL (4.83 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.5 mg/mL (4.83 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.5 mg/mL (4.83 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

MRK-560 is an orally active, brain barrier-penetrating γ-Secretase inhibitor, can potently reduces Aβ peptide in rat brain and cerebrospinal fluid. MRK-560 also decreases mutant NOTCH1 processing by selectively inhibiting PSEN1. MRK-560 can be used in studies of Alzheimer's disease and T-cell acute lymphoblastic leukaemia (T-ALL)<sup>[1][2]</sup>.

#### IC<sub>50</sub> & Target

PSEN1

#### In Vitro

MRK-560 (30, 100, 300, 1000 nM; 15days) blocks mutant NOTCH1 receptor signaling in human T-ALL cell lines<sup>[1]</sup>.

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

#### Cell Proliferation Assay<sup>[1]</sup>

Cell Line:	HPB-ALL, DND-41, and Jurkat cells
Concentration:	30, 100, 300, 1000 nM
Incubation Time:	15 days
Result:	Reduced NICD1 generation in cells and resulted in a dose-dependent decrease of proliferation in HPB-ALL and DND-41, which depend on NOTCH signaling for their survival.

#### In Vivo

MRK-560 (15.54 mg/kg; S.C.; single daily for 14 days) shows strong antileukemic effects on T-ALL model<sup>[1]</sup>.  
MRK-560 (1, 3, 10, 30, 100 mg/kg; p.o.; single) shows good blood-brain barrier permeability in a dose-dependent manner in rats<sup>[2]</sup>.

MRK-560 (1, 3, 10, 30, 100 mg/kg; p.o.; single) inhibits the production of A $\beta$  levels in brain and cerebrospinal fluid<sup>[2]</sup>.

MRK-560 (1 mg/kg; p.o.; single) shows a good bioavailability of 70 to 90%, and T<sub>max</sub> is 12 h<sup>[2]</sup>.

MRK-560 (1 mg/kg; i.v.; single) is suitable for once-a-day dosing (with a low plasma clearance and a half-life of more than 15 h)<sup>[2]</sup>.

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

Animal Model:	Tg (HLA-DRB1) 31Dmz/Szj (NSG) mice (T-ALL (T cell acute lymphoblastic leukemia) model) <sup>[1]</sup> .
Dosage:	15.54 mg/kg
Administration:	Subcutaneous injection; single daily for 14 days.
Result:	Resulted in strong antileukemic effects and improved median survival to 30 days compared to 18 days in vehicle-treated mice.

Animal Model:	Male Sprague-Dawley rats (250-300 g) <sup>[2]</sup> .
Dosage:	1, 3, 10, 30, 100 mg/kg
Administration:	Oral administration; single (experiment is performed 8 h later)
Result:	Increased the plasma and brain concentrations in a dose-dependent manner. Reduced (dose-dependent) both brain and CSF A $\beta$ levels, with essentially complete inhibition of the production of both peptides being observed at a dose of 100 mg/kg.

Animal Model:	Male Sprague-Dawley rats (250-300 g) <sup>[2]</sup> .
Dosage:	1 mg/kg
Administration:	Intravenously and orally administration; single.
Result:	Showed T <sub>max</sub> after the oral dose was 12 h, and bioavailability was 70 to 90%. Revealed a low plasma clearance of less than 5 mL/min/kg with a volume of distribution of approximately 6 L/kg, which translated to a long half-life of more than 15 h.

## REFERENCES

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[1]. Habets RA, et al. Safe targeting of T cell acute lymphoblastic leukemia by pathology-specific NOTCH inhibition. *Sci Transl Med.* 2019 May 29;11(494):eaau6246.

[2]. Best JD, et al. In vivo characterization of Abeta(40) changes in brain and cerebrospinal fluid using the novel gamma-secretase inhibitor N-[cis-4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexyl]-1,1,1-trifluoromethanesulfonamide (MRK-560) in t

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

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