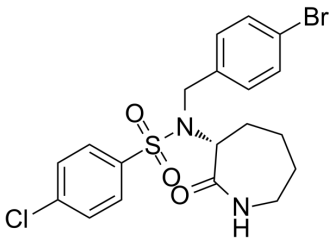
ELN318463

Cat. No.:	HY-50882
CAS No.:	851600-86-7
Molecular Formula:	$C_{19}H_{20}BrClN_2O_3S$
Molecular Weight:	471.8
Target:	γ-secretase
Pathway:	Neuronal Signaling; Stem Cell/Wnt
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (264.94 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1195 mL	10.5977 mL	21.1954 mL
	5 mM	0.4239 mL	2.1195 mL	4.2391 mL
	10 mM	0.2120 mL	1.0598 mL	2.1195 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: ≥ 2.08 mg/mL (4.41 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ELN318463 is an amyloid precursor protein (APP) selective γ-secretase inhibitor. ELN318463 shows differential inhibition of presenilin (PS1)- and PS2-comprised γ-secretase with EC_{50}s of 12 nM and 656 nM for PS1 and PS2, respectively. ELN318463 is 51-fold more selective for PS1[1][2].

IC_{50} & Target

EC50: 12 nM (PS1 γ-secretase), 656 nM (PS2 γ-secretase)[1]

In Vitro

ELN318463 behaves as a classic γ-secretase inhibitor, demonstrates 75- to 120-fold selectivity for inhibiting Aβ production compared with Notch signaling in cells, and displaces an active site directed inhibitor at very high concentrations only in the presence of substrate[2].

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

In Vivo	ELN318463 (30 mg/kg or 100 mg/kg; orally) leads acute reduction of brain Aβ in in the PDAPP transgene model of Alzheimer's disease (AD) as well as in wild-type FVB strain mice[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female, two- to three-month old, FVB/N mice and PDAPP transgene model of Alzheimer's disease (AD)[2]
Dosage:	30 mg/kg or 100 mg/kg
Administration:	Orally
Result:	Brain levels at 30 mg/kg were 0.754 μM in FVB brains and 0.69 μM in PDAPP brains, and at 100 mg/kg dose the levels were 2.7 μM in FVB brains and 1.87 μM in PDAPP brains.

REFERENCES

[1]. Zhao B, et al. Identification of gamma-secretase inhibitor potency determinants on presenilin. J Biol Chem. 2008 Feb 1;283(5):2927-38.

[2]. Basi GS, et al. Amyloid precursor protein selective gamma-secretase inhibitors for treatment of Alzheimer's disease. Alzheimers Res Ther. 2010 Dec 29;2(6):36.

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