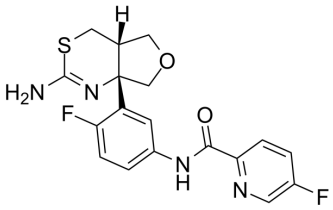
LY2886721

Cat. No.:	HY-13240
CAS No.:	1262036-50-9
Molecular Formula:	$C_{18}H_{16}F_2N_4O_2S$
Molecular Weight:	390.41
Target:	Beta-secretase
Pathway:	Neuronal Signaling
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 16.67 mg/mL (42.70 mM)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5614 mL	12.8070 mL	25.6141 mL
5 mM	0.5123 mL	2.5614 mL	5.1228 mL
10 mM	0.2561 mL	1.2807 mL	2.5614 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2 mg/mL (5.12 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LY2886721 is a potent, selective and orally active beta-site amyloid precursor protein cleaving enzyme 1 (BACE1) inhibitor with an IC_{50} of 20.3 nM for recombinant human BACE1. LY2886721 is selectivity against cathepsin D, pepsin, and renin, but lacking selectivity against BACE2 (IC_{50} of 10.2 nM). LY2886721 can across blood-brain barrier and has the potential for Alzheimer's disease treatment[1].

IC_{50} & Target

IC50: 20.3 nM (Beta-site amyloid precursor protein cleaving enzyme 1 (BACE1)); 10.2 nM (BACE2)[1]

In Vitro

Overnight exposure of HEK293Swe cells to increasing concentrations of LY2886721 shows a concentration-dependent decrease in the amount of Aβ secreted into the condition medium. Consistent with a mechanism of BACE inhibition, the EC_{50} s for inhibition of $Aβ_{1-40}$ and $Aβ_{1-42}$ are essentially identical, 18.5 and 19.7 nM, respectively[1].

Overnight exposure of PDAPP neuronal cultures to an increasing concentration of LY2886721 produces a concentration-

dependent decrease in Aβ production. As observed in HEK293Swe cells, the EC_{50}s for inhibition of $Aβ_{1-40}$ and $Aβ_{1-42}$ are comparable in PDAPP neuronal cultures at ~10 nM[1].

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

In Vivo

LY2886721 (3-30 mg/kg; oral administration; PDAPP mice) treatment significantly reduces the hippocampal and cortical levels of $Aβ_{1-X}$. LY2886721 treatment results in significant reduction of brain parenchymal levels of C99 and sAPPβ[1].

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

Animal Model:	Female hemizygous APPV717F transgenic mice (PDAPP) (2-3 months old)[1]
Dosage:	3 mg/kg, 10 mg/kg, 30 mg/kg
Administration:	Oral administration
Result:	Hippocampal and cortical levels of $Aβ_{1-X}$ were significantly reduced.

CUSTOMER VALIDATION

- Cell Rep. 2020 Jun 2;31(9):107719.
- FASEB J. 2021 May;35(5):e21445.

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REFERENCES

[1]. May PC1, et al. The potent BACE1 inhibitor LY2886721 elicits robust central Aβ pharmacodynamic responses in mice, dogs, and humans. J Neurosci. 2015 Jan 21;35(3):1199-210.

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