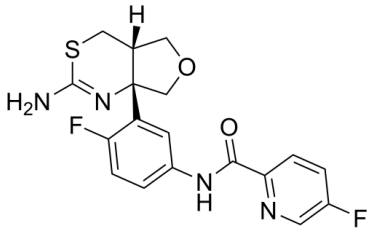
Data Sheet

Product Name:	LY2886721
Cat. No.:	CS-0458
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
Solubility:	DMSO : ≥ 16.67 mg/mL



BIOLOGICAL ACTIVITY:

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]. IC50 & 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]. ***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].

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.

CAIndexNames:

2-Pyridinecarboxamide, N-[3-[(4aS,7aS)-2-amino-4a,5-dihydro-4H-furo[3,4-d][1,3]thiazin-7a(7H)-yl]-4-fluorophenyl]-5-fluoro-

SMILES:

FC1=CN=C(C=C1)C(NC2=CC=C(C([C@@]34[C@]([H])(CSC(N)=N4)COC3)=C2)F)=O

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

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