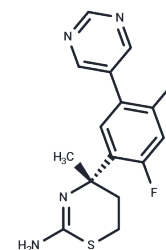


LY2811376

Chemical Properties

CAS No. : 1194044-20-6
 Formula: C₁₅H₁₄F₂N₄S
 Molecular Weight: 320.36
 Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
 Actual storage temperature shall be subject to the COA.



Biological Description

Description	LY2811376, an orally available non-peptidic β -secretase(BACE1) inhibitor (IC ₅₀ : 239-249 nM), can decrease A β secretion (EC ₅₀ : 300 nM). It has 10-fold selectivity towards BACE1 over BACE2, and more than 50-fold inhibition over other aspartic proteases including pepsin, cathepsin D, or renin.
Targets(IC ₅₀)	Beta Amyloid,Beta-Secretase,BACE
In vitro	In the APPV717F mouse model of A β pathology, LY2811376 (10/30/100 mg/kg) induced a dose-dependent significant reduction in A β , sAPP β , and C99, which are the closest breakdown products following the hydrolysis of APP by BACE1 protein. In beagle dogs, LY2811376 (5 mg/kg) resulted in a decrease in plasma A β 1-x levels, with the maximum reduction of 85% occurring between 4-12 hours post-administration.
In vivo	LY2811376 exhibits a concentration-dependent reduction in the secretion of A β in HEK293 cells overexpressing APP. It also concentration-dependently inhibits hBACE1, including small synthetic peptide substrates (IC ₅₀ : 239 nM) and larger chimeric protein substrates (IC ₅₀ : 249 nM). In primary neuronal cultures from PDAPP transgenic mice, LY2811376 inhibits A β secretion (EC ₅₀ : 100 nM).
Kinase Assay	Determination of enzymatic efficiency: The stock solution for each FRET peptide substrate is prepared at 30 mM in dimethylsulfoxide (DMSO). The huBACE1:Fc muBACE1:Fc preparation is concentrated through YM10 Centricon. to a final concentration of at least 7 mg/mL. The optimal enzyme concentration for each FRET peptide substrate is determined individually at 30 μ M FRET peptide substrate in 50 mM ammonium acetate, pH 4.6, 1 mg/mL BSA and 1 mM Triton X-100. The enzymatic efficiency (k _{cat} /K _m) of either of the BACE1 orthologs toward individual FRET peptide substrates at 15, 30 and 100 μ M is determined under the optimal conditions for each substrate. The progress of the reaction is monitored by measuring an increase of the emission signal at 420 nm with excitation wavelength set at 320 nm, using a GEMINI fluorescence plate reader. Amino acid conjugated aminobenzoate is used to convert the emission signal in the relative fluorescence units into the molar concentration of product generated in the reaction mixture. The initial phase of the time dependence curve is fitted with a linear function whose slope is used to calculate the initial rate for huBACE1:Fc toward each peptide substrate. The k _{cat} /K _m values are calculated from the linear dependence of the initial rate on the concentration of each peptide.

A DRUG SCREENING EXPERT

Cell Research	The cytotoxicity in the HEK293Swe cell model is assessed using a CellTiter 96 Aqueous Non-Radioactive Cell Proliferation Assay. (Only for Reference)
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Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 13 mg/mL (40.58 mM),Sonication is recommended. Ethanol: 60 mg/mL (187.29 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (6.24 mM),Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.1215 mL	15.6074 mL	31.2149 mL
5 mM	0.6243 mL	3.1215 mL	6.243 mL
10 mM	0.3121 mL	1.5607 mL	3.1215 mL
50 mM	0.0624 mL	0.3121 mL	0.6243 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

May P, et al. J Neurosci, 2011, 31(46), 16507-16516.

Yang HC, et al. J Neurochem, 2004, 91(6), 1249-1259.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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