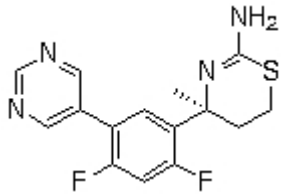
Product Introduction

LY2811376

LY2811376 is the first orally available non-peptidic **β-secretase(BACE1)** inhibitor with **IC50** of 239 nM-249 nM, that act to decrease Aβ secretion with **EC50** of 300 nM, demonstrated to have 10-fold selectivity towards BACE1 over BACE2, and more than 50-fold inhibition over other aspartic proteases including cathepsin D, pepsin, or renin. Phase 1.

Technical Data:

Molecular Weight (MW):	320.36	
Formula:	$C_{15}H_{14}F_2N_4S$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 16 mg/mL	
	Water <1 mg/mL	
	Ethanol 64 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	1194044-20-6	

Biological Activity

LY2811376 demonstrates concentration-dependent inhibition of hBACE1 with an IC50 of 239 and 249 nM against a small synthetic peptide or a larger chimeric protein substrate, respectively. LY2811376 treatment yields a concentration-dependent decrease in Aβ secretion in APP-overexpressing HEK293 cells.

LY2811376 inhibits Aβ secretion with EC50 of ~100 nM in primary neuronal cultures of PDAPP transgenic mouse. [1]

Administration of LY2811376 (10, 30, and 100 mg/kg doses) results in dose-dependent, significant reductions in Aβ, as well as sAPPβ and C99, the proximal cleavage products of APP proteolysis by BACE1 in APP^{V717F} mouse model of Aβ pathology. After treatment with LY2811376 (5 mg/kg), reductions in $Aβ_{1-x}$ are observed in plasma, with a maximal 85% reduction observed from 4 to 12 h after dosing in beagle dogs. [1]

Approximately 10-fold selectivity toward BACE1 over BACE2.

References

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

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

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