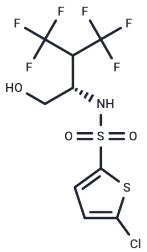
Data Sheet (Cat.No.T14525)

TargetMol

Begacestat

Chemical Properties



CAS No. : 769169-27-9

Formula: C9H8ClF6NO3S2

Molecular Weight: 391.74

Storage: Store at low temperature
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	Begacestat (GSI-953) is a potent and selective gamma-secretase inhibitor (γ-secretase) that inhibits Amyloid-beta production with nanomolar potency, selectively inhibits cleavage of APP in cellular level Notch cleavage assays, reverses situational memory deficits, and can be used to study Alzheimer's disease.
Targets(IC50)	Beta Amyloid,Gamma-secretase
In vitro	In CHO cells overexpressing human APP, Begacestat inhibited Aβ42 with an IC_{50} of 10 nM and Aβ40 with an IC_{50} of 6 nM after 16 hours of treatment. In HeLa cells, the IC_{50} for endogenous Aβ inhibition was 3 nM. Begacestat has reduced potency against Notch signaling, with an IC_{50} of 74 nM for Notch cleavage, indicating selectivity between Aβ and Notch inhibition[2].
In vivo	In Tg2576 transgenic mice, oral administration (p.o.) of Begacestat resulted in a significant reduction of brain Aβ levels at 3 hours post-dose. A single 10 mg/kg dose led to a 60% reduction in Aβ40 and a 54% reduction in Aβ42 in brain tissue. In Sprague-Dawley rats, a 30 mg/kg oral dose produced a 78% reduction in brain Aβ levels after 4 hours[2].

Solubility Information

Solubility	DMSO: 40 mg/mL (102.11 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 (5.11 mM),Sonication is recommended. *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.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5527 mL	12.7636 mL	25.5271 mL
5 mM	0.5105 mL	2.5527 mL	5.1054 mL
10 mM	0.2553 mL	1.2764 mL	2.5527 mL
50 mM	0.0511 mL	0.2553 mL	0.5105 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

Mayer SC, et al. Discovery of begacestat, a Notch-1-sparing gamma-secretase inhibitor for the treatment of Alzheimer's disease. J Med Chem. 2008 Dec 11;51(23):7348-51.
Martone RL, et al. Begacestat (GSI-953): a novel, selective thiophene sulfonamide inhibitor of amyloid precursor protein gamma-secretase for the treatment of Alzheimer's disease. J Pharmacol Exp Ther. 2009 Nov;331(2):598-608.