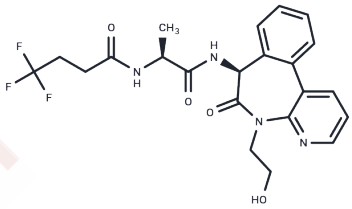
Data Sheet (Cat.No.T3633)

TargetMol

Crenigacestat

Chemical Properties



CAS No. : 1421438-81-4

Formula: C22H23F3N4O4

Molecular Weight: 464.44

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Crenigacestat (LY3039478) is an orally bioavailable Notch inhibitor with an IC50 of ~1 nM in most tumor cell lines tested. It effectively inhibits mutant Notch receptor activity and, in a xenograft tumor model, inhibits the expression of Notch-regulated genes and N1ICD cleavage in the tumor microenvironment.
Targets(IC50)	Gamma-secretase
In vitro	Crenigacestat is a novel small molecule that is an exquisitely potent inhibitor of Notch-1 intracellular domain (N1ICD) cleavage with an IC50 of ~ 1 nM in most of the tumor cell lines tested. Crenigacestat also potently inhibits mutant Notch receptor activity[2]. Treatment with a gamma secretase inhibitor, Crenigacestat, significantly inhibited the growth of 2 CCRCC(Clear cell renal cell carcinoma) cell lines in a concentration dependent manner. Crenigacestat treatment also led to decreased expression of Myc and Cyclin A1, two genes that were part of the NOTCH driven proliferative signature in murine and human model systems. Crenigacestat treatment also led to G0/G1 cell cycle arrest in CCRCC cells[3].
In vivo	In mice, its oral bioavalability(%F) is 65%, clearance(CL)=41 mL/min/kg, VDss = 3.8 L/kg. In Rats, its oral bioavalability(%F) is 65%, CL=98 mL/min/kg, VDss=4.9 L/kg. In Dogs, its oral bioavalability (%F) is 67%, CL=3.8 mL/min/kg, VDss=1.4 L/kg[1]. In a xenograft tumor model, Crenigacestat inhibited N1ICD cleavage and expression of Notch-regulated genes in the tumor microenvironment. The inhibition of Notch cleavage also resulted in the induction of apoptosis in a Notch-dependent xenograft model[2]. In immunodeficient NSG mice xenografted with 769-P CCRCC cells, Crenigacestat treatment resulted in significantly increased survival and delayed tumor growth in independent cohorts of mice demonstrating in vivo efficacy in CCRCC[3].
Cell Research	K07074 cells were plated to 24-well plates at 10⁵ cell/well. Viability of cells was assessed in quadruplicates at indicated timepoints using the CellTiter-Glo luminescent cell viability assay. To study the effect of the small molecular compounds on K07074 cell growth the compounds or DMSO were added to the growth media 24 h after seeding. The cells were incubated with inhibitors and DMSO as indicated. Cell viability was assessed as described above. Each experiment was carried out in triplicate and at least 3 independent experiments were performed. (Only for Reference)

Solubility Information

Solubility	DMSO: 55 mg/mL (118.42 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1531 mL	10.7657 mL	21.5313 mL
5 mM	0.4306 mL	2.1531 mL	4.3063 mL
10 mM	0.2153 mL	1.0766 mL	2.1531 mL
50 mM	0.0431 mL	0.2153 mL	0.4306 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.

Reference

Eli Lilly Company. The 8th SCI-RSC Symposium on Proteinase Inhibitor Design. 2013.
Lu B, He Y, He J, et al. Epigenetic profiling identifies LIF as a super-enhancer controlled regulator of stem cell-like properties in osteosarcoma. Molecular Cancer Research. 2020, 18(1): 57-67
Mark H. Bender, et al. Cancer Res, 2013, 73(8 Suppl):Abstract nr 1131.
Bhagat TD, et al. J Biol Chem. 2017, 292(3):837-846.
Mäemets-Allas K, et al. Biochem Biophys Res Commun. 2016 May 20;474(1):118-25.
Lu B, He Y, He J, et al. Epigenetic Profiling Identifies LIF as a Super-enhancer-Controlled Regulator of Stem Cell-like Properties in Osteosarcoma[J]. Molecular Cancer Research. 2020, 18(1): 57-67.