Crenigacestat

Cat. No.: HY-12449

CAS No.: 1421438-81-4

Molecular Formula: $C_{22}H_{23}F_3N_4O_4$

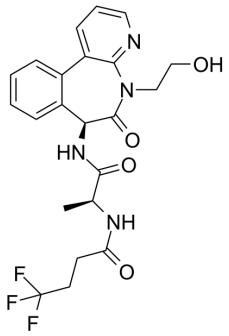
Molecular Weight: 464.44

Target: Notch; γ-secretase

Pathway: Neuronal Signaling; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 34 mg/mL (73.21 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Crenigacestat (LY3039478) is an orally active Notch and γ-secretase inhibitor, with an IC_{50} of 1 nM in most of the tumor cell lines tested[1][2][3][4].

In Vitro

Crenigacestat (100 nM) exhibits anti-cancer activity in K07074 cells (a primary mouse liver tumor cell line)[2].
Crenigacestat (LY3039478) decreases expression of Myc and cyclin A1 (part of the NOTCH-driven proliferative signature) in murine and human model systems. Crenigacestat (LY3039478) treatment also leads to G0/G1 cell cycle arrest in CCRCC cells

[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2].

Cell Line:	K07074 cells.
Concentration:	100 nM.
Incubation Time:	24-96 hours.
Result:	Effectively reduced the growth of K07074 cells.

In Vivo

Crenigacestat (8 mg/kg, oral gavage three times a week) resulted in significantly increases survival and delayed tumor growth in independent cohorts of mice demonstrating in vivo efficacy in CCRCC[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	CCRCC xenografts were established in NOD-scid IL2R null mice with subcutaneous implantation using the 769-P cell line[3].
Dosage:	8 mg/kg.
Administration:	Oral gavage three times a week.
Result:	Resulted in increased overall survival when compared with vehicle control in CCRCC xenografts.

CUSTOMER VALIDATION

- Cell Mol Immunol. 2022 Oct 14.
- Nat Commun. 2022 Nov 29;13(1):7341.
- J Cell Biochem. 2018 Oct 28.
- ACS Comb Sci. 2019 Dec 9;21(12):805-816.

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REFERENCES

[1]. Yuen E, et al. Evaluation of the effects of an oral notch inhibitor, crenigacestat (LY3039478), on QT interval, and bioavailability studies conducted in healthy subjects. Cancer Chemother Pharmacol. 2019 Mar;83(3):483-492.

[2]. Mäemets-Allas K, et al. The inhibition of Akt-Pdpk1 interaction efficiently suppresses the growth of murine primary liver tumor cells. Biochem Biophys Res Commun. 2016 May 20;474(1):118-125.

[3]. Bhagat TD, et al. Notch Pathway Is Activated via Genetic and Epigenetic Alterations and Is a Therapeutic Target in Clear Cell Renal Cancer. J Biol Chem. 2017 Jan 20;292(3):837-846.

[4]. Mark H. Bender, et al. Abstract 1131: Novel inhibitor of Notch signaling for the treatment of cancer. Experimental and Molecular Therapeutics. 2013.

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

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