产品名称：LY3039478
产品别名：Crenigacestat

生物活性：

Description	Crenigacestat is an orally active Notch and γ-secretase inhibitor, with an IC50 of ~1nM 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].
	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].
	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.

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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (5.38 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.38 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.38 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.