产品名称：**EPZ011989**
产品别名：**EPZ011989**

生物活性：

Description

EPZ011989 is a potent, selective orally bioavailable EZH2 inhibitor with Ki < 3 nM for EZH2 wt and EZH2 Y646; 15-fold selectivity over EZH1 and >3000-fold selectivity over other HMTase. IC50 value: < 3 nM (Ki for wt EZH2, EZH2 Y646) Target: EZH2 inhibitor In vitro: EPZ011989 is also a specific EZH2 inhibitor with a >15-fold selectivity over EZH1 and >3000-fold selectivity relative to the Ki of 20 other histone methyltransferases (HMTs) tested. EPZ011989 also exhibits metabolic stability. Furthermore, EPZ011989 reduces cellular H3K27 methylation in the Y641F, mutant-bearing human lymphoma cell line, WSU-DLCL2, with an IC50 below 100 nM. This functional response translates to activity in a long-term proliferation assay where EPZ011989 demonstrates an average lowest cytotoxic concentration (LCC) in WSU-DLCL2 cells of 208 nM. In vivo: The LCC parameter, when corrected for plasma protein-binding, predicts an efficacious plasma level in mouse for EPZ011989 of 158 ng/mL. The pharmacokinetics in SCID mice following oral administration of 125, 250, 500, and 1000 mg/kg indicated that the 1000 mg/kg dose provided coverage over the LCC for 24 h, while the 250 and 500 mg/kg doses provided coverage over this value for approximately 8 h. EPZ011989 demonstrates significant tumor growth inhibition in a mouse xenograft model of human B cell lymphoma.

Solvent&Solubility

In Vitro:

DMSO : 100 mg/mL (**165.07 mM**; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6507 mL	8.2534 mL	16.5068 mL
	5 mM	0.3301 mL	1.6507 mL	3.3014 mL
	10 mM	0.1651 mL	0.8253 mL	1.6507 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 (4.13 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.13 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 (4.13 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.13 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 (4.13 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.13 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]. Campbell JE, et al. EPZ011989, A Potent, Orally-Available EZH2 Inhibitor with Robust in Vivo Activity. ACS Med Chem Lett. 2015 Mar 4;6(5):491-495.