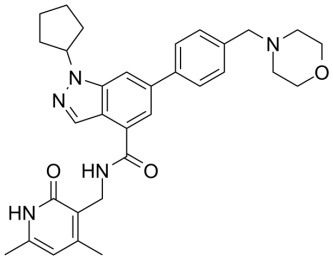
EPZ005687

Cat. No.:	HY-15555
CAS No.:	1396772-26-1
Molecular Formula:	$C_{32}H_{37}N_5O_3$
Molecular Weight:	539.67
Target:	Histone Methyltransferase
Pathway:	Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 9.4 mg/mL (17.42 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8530 mL	9.2649 mL	18.5298 mL
	5 mM	0.3706 mL	1.8530 mL	3.7060 mL
	10 mM	0.1853 mL	0.9265 mL	1.8530 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: ≥ 1.67 mg/mL (3.09 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (3.09 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (3.09 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

EPZ005687 is a potent and selective inhibitor of EZH2 with K_i of 24 nM, and has 50-fold selectivity against EZH1 and 500-fold selectivity against 15 other protein methyltransferases.

IC_{50} & Target

EZH2
24 nM (Ki)

In Vitro

EPZ005687 shows concentration-dependent inhibition of PRC2 enzymatic activity with an IC_{50} value of 54±5 nM. EPZ005687

specifically inhibits H3K27 methylation in lymphoma cells. EPZ005687 has a notable effect on proliferation of the EZH2Y641F-bearing cell line. EPZ005687 decreases proliferation in mutant but not wild-type EZH2 lymphoma cells[1]. EPZ005687 (0.5, 1, 5 and 10 μM) induces an obvious apoptosis of U937 cells in a dose-dependent manner. EPZ005687 inhibits obviously the proliferation of U937 cells but has weak effect on the proliferation of NBMCD34$^+$ cells. EPZ005687 induces G1 phase blocking and decreases the percentage of cells in S phase in U937 cells. In addition, EPZ005687 produces obviously depletion of H3K27 methylation in U937 cells, but hardly has effect on the H3K27 methylation of NBMCD34$^+$ cells[2].

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

PROTOCOL

Kinase Assay [1]

10-point curves of EPZ005687 are made using serial 3-fold dilution in DMSO, beginning at 2.5 mM (final top concentration of compound is 50 μM and the DMSO is 2%). A 1 μL aliquot the inhibitor dilution series is spotted in a 384-well microtiter plate. The 100% inhibition control consisted of 1 mM final concentration of the product inhibitor S-adenosylhomocysteine (SAH). Compound is incubated for 30 min with 40 μL per well of 5 nM PRC2 (final assay concentration in 50 μL is 4 nM) in 1X assay buffer (20 mM Bicine [pH 7.6], 0.002% Tween 20, 0.005% Bovine Skin Gelatin and 0.5 mM DTT). 10 μL per well of substrate mix comprising assay buffer ^{3}H-SAM, unlabeled SAM, and peptide representing histone H3 residues 21-44 containing C-terminal biotin (appended to a C-terminal amide-capped lysine) are added to initiate the reaction. Reactions are incubated for 90 min at room temperature and quenched with 10 μL per well of 600 μM unlabeled SAM, then transferred to 384-well Flashplate and washed after 30 min.

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Cell Assay [1]

For cell cycle, WSU-DLCL2 cells are plated in 12-well plates at a density of 1×10^5 cells per mL. Cells are incubated with EPZ005687 at 0.2 μM, 0.67 μM, 2 μM and 6 μM, in a total of 2 mL, over a course of 10 d. All remaining cell cycle analysis is performed.

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

CUSTOMER VALIDATION

- Cell Syst. 2018 Apr 25;6(4):424-443.e7.
- Free Radic Biol Med. 2017 Mar 16;108:280-299.
- Sci Rep. 2016 Aug 19;6:29176.
- J Oncol. 2022 Jun 23;2022:8724933.
- Patent. US20180263995A1.

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REFERENCES

[1]. Knutson SK, et al. A selective inhibitor of EZH2 blocks H3K27 methylation and kills mutant lymphoma cells. Nat Chem Biol. 2012;8(11):890-6.

[2]. Tang SH, et al. Effects of H3K27 methylation inhibitor EPZ005687 on apoptosis, proliferation and cell cycle of U937 cells and normal CD34 positive cells. Zhongguo Shi Yan Xue Ye Xue Za Zhi. 2014 Dec;22(6):1561-6.

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

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