

Pinometostat

Chemical Properties

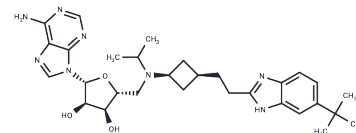
CAS No. : 1380288-87-8

Formula: C30H42N8O3

Molecular Weight: 562.71

Appearance: no data available

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



Biological Description

Description	Pinometostat (EPZ-5676) has been used in trials studying the treatment of Leukemia, Acute Leukemias, Acute Myeloid Leukemia, Myelodysplastic Syndrome, and Acute Lymphocytic Leukemia, among others.
Targets(IC50)	Histone Methyltransferase
In vitro	At its highest dosage of 70.5 mg/kg/day, EPZ-5676 effectively induced complete remission of tumors, with no regrowth observed for up to 32 days following cessation of treatment. Rats treated with EPZ-5676 did not exhibit significant weight loss or apparent toxicity. A continuous intravenous infusion of EPZ-5676 over 21 days into a xenograft model of MLL-rearranged leukemia demonstrated dose-dependent antitumor activity.
In vivo	Treatment with EPZ-5676 results in a concentration- and time-dependent reduction in H3K79 methylation without affecting the methylation status of other histone sites. This leads to the suppression of key MLL target genes and induces selective apoptotic cell death in MLL-rearranged leukemia cells. Specifically, in MV4-11 cells, EPZ-5676 decreases dimethylation of H3K79, with a cell IC50 of 2.6 nM. Additionally, EPZ-5676 inhibits the proliferation of the MLL-AF4 rearranged cell line MV4-11, with an IC50 of 9 nM.
Cell Research	EPZ-5676 is dissolved in DMSO. To analyse inhibition of histone methylation in MV4-11 cells following EPZ-5676 treatment, extracted histones (400 ng) are fractionated on a 10-20% Tris HCl gels with Tris-Glycine SDS running buffer under denaturing conditions and transferred to nitrocellulose filters. Filters are cut into strips and incubated for 1 hour in blocking buffer at room temperature (RT) and then incubated overnight at 4°C in blocking buffer. Filters are washed 3 times for 5 minutes with wash buffer (Phosphate buffered saline (PBS) including 0.01% Tween 20 (PBST)) and incubated with infrared tagged secondary antibody at RT for 1 hour. Filters are washed in PBST and reprobed for 1 hour at RT with the appropriate total histone antibody control (mouse anti-histone H3 (1:20,000), CST 3638, or mouse anti-histone H4 (1:10,000), CST 2935). Filters are washed again in PBST and incubated with infrared tagged secondary antibody (IRDye 800Cw donkey-anti-mouse IgG (1:20,000), Li-Cor 926-32212) at RT for 1 hour. After a final wash in PBST, filters are scanned using the Odyssey infrared imager (Li-cor). To analyse inhibition of H3K79 methylation in peripheral blood mononuclear cells (PBMCs) from rats dosed with EPZ-5676, 20 µL of PBMC whole cell lysate is fractionated on denaturing gels and analysed by immunoblotting with antibodies to H3K79me2 or total H3. Signal intensities specific for the H3K79me2 antibody and total histone H3 control antibody are quantified

using Odyssey software. The H3K79me2 signal intensity is normalized by dividing it by the total histone H3 control signal intensity in the same lane.

Solubility Information

Solubility	Ethanol: 85 mg/mL (151.1 mM), DMSO: 60 mg/mL (106.63 mM), (< 1 mg/ml refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.7771 mL	8.8856 mL	17.7711 mL
5 mM	0.3554 mL	1.7771 mL	3.5542 mL
10 mM	0.1777 mL	0.8886 mL	1.7771 mL
50 mM	0.0355 mL	0.1777 mL	0.3554 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

Robert A. Protein methyltransferases in cancer. AACR Annual Meeting, 2013.

Yu S, Zhou C, He J, et al. BMP4 drives primed to naïve transition through PGC-like state. Nature Communications.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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