

Product Data Sheet

Product Name: EPZ5676

Cat. No.: GC12932

Chemical Properties

Cas. No. 1380288-87-8

Chemical Name (2R,3S,4S,5R)-2-(6-aminopurin-9-yl)-5-[[[3-[2-(6-tert-butyl-1H-benzimidazol-2-yl)ethyl]cyclobutyl]-propan-2-ylamino]methyl]oxolane-3,4-diol

SMILES CC(C)N(CC1C(C(C(O1)N2C=NC3=C2N=CN=C3N)O)O)C4CC(C4)CCC5=NC6=C(N5)C=C(C=C6)C(C)(C)C

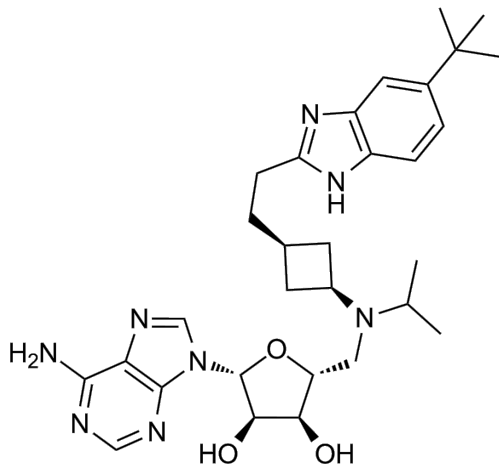
Formula $C_{30}H_{42}N_8O_3$ M.Wt 562.71

Solubility ≥ 28.15 mg/mL in DMSO, ≥ 50.3 mg/mL in EtOH with ultrasonic Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Cell lines	MCF7 cells (human ER-positive/HER2-negative breast cancer cell line) and SKBR3 cells (human ER-negative/HER2-positive breast cancer cell line)
Preparation Method	MCF7 and SKBR3 cells were treated with EPZ5676 (1 μ M) for up to 15 days, replacing the medium and drug every 3 days.
Reaction Conditions	1 μ M; 6-15 days.
Applications	EPZ5676 significantly suppressed colony formation and induced cell cycle arrest (G1 arrest in MCF7 cells) and apoptosis in both breast cancer cell lines. EPZ5676 also activated interferon signaling, upregulated HLA class I expression, and induced DNA damage.

Animal experiment [2]:

Animal models	C57BL/6 mice with <i>P. acnes</i> /LPS-induced fulminant hepatitis
Preparation Method	Mice were intraperitoneally administered EPZ5676 (35mg/kg) on days 0, 2, 4, and 6 after <i>P. acnes</i> priming, followed by LPS injection on day 7 to induce fulminant hepatitis. Mice were monitored for survival and sacrificed for analysis at day 7.
Dosage form	35mg/kg; i.p.; Four injections over 6 days.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Applications EPZ5676 treatment significantly improved survival rates, attenuated liver injury severity, reduced hepatic granuloma formation, and decreased hepatocyte apoptosis in fulminant hepatitis mice. EPZ5676 also enhanced the immunosuppressive function of myeloid-derived suppressor cells (MDSCs) through epigenetic regulation of the SOCS1-iNOS pathway.

References:

- [1] W Yang W, Yu H, Huang J, et al. Inhibition of Dot1L Alleviates Fulminant Hepatitis Through Myeloid-Derived Suppressor Cells. *Cell Mol Gastroenterol Hepatol*. 2021;12(1):81-98.
- [2] Yoshido A, Ishiguro K, Kitajima H, et al. DOT1L inhibition exerts the anti-tumor effect by activating interferon signaling in breast cancer cells. *Clin Epigenetics*. 2025 Nov 26;17(1):201.

Background

EPZ5676 is a novel, highly potent and selective DOT1L histone methyltransferase inhibitor with a K_i value of less than 80pM and an IC_{50} of 0.8nM against DOT1L, showing selectivity that is 37,000-fold higher than against other protein methyltransferases^[1-2]. EPZ5676 inhibits H3K79 methylation and the expression of MLL fusion target genes. EPZ5676 is used in research related to mixed-lineage leukemia (MLL-rearranged leukemia) ^[3-4].

In vitro, EPZ5676 (1 μ M) was used to treat estrogen receptor-positive/HER2-negative breast cancer cells (MCF7) and estrogen receptor-negative/HER2-positive cells (SKBR3) for 15 days. EPZ5676 significantly inhibited the levels of mono-, di-, and trimethylation of histone H3K79, effectively suppressed colony formation in both breast cancer cell lines, induced cell cycle G1 phase arrest and apoptosis, while also activating the interferon signaling pathway and upregulating HLA class I molecule expression^[5]. EPZ5676 (0-3 μ M) was also used to treat HeLa cells, Molm-13 cells, and MV4-11 cells for 72 hours. EPZ5676 resulted in significant inhibition of histone H3K79 dimethylation levels (IC_{50} =7nM), HoxA9 promoter activity (IC_{50} =52nM), and proliferation of MLL-rearranged leukemia cells (IC_{50} =15nM)^[6].

In vivo, in a *P. acnes*/LPS-induced fulminant hepatitis model, EPZ5676 (35mg/kg/day) was

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

administered intraperitoneally to C57BL/6 mice (starting from day 0 after infection, once every two days, for a total of four times). EPZ5676 significantly improved mouse survival, alleviated liver injury and immune cell infiltration, and enhanced the immunosuppressive function of myeloid-derived suppressor cells (MDSCs)^[7]. In a TNBC xenograft model, EPZ5676 (50mg/kg) was administered intraperitoneally to tumor-bearing (MDA-MB-468 cells) NSG mice (once every other day, for a total of six times). EPZ5676 significantly reduced the frequency of tumor-initiating cells, inhibited tumor growth and metastasis, and decreased the proportion of ALDH1+ cancer stem cells^[8].

References:

- [1] Daigle SR, Olhava EJ, Therkelsen CA, et al. Potent inhibition of DOT1L as treatment of MLL-fusion leukemia. *Blood*. 2013 Aug 8;122(6):1017-25.
- [2] Choi HJ, Nguyen MT, Kim B, et al. DOT1L as a Therapeutic Target: Insights into Epigenetic Regulation and Cancer Treatment. *Biomol Ther (Seoul)*. 2025 Nov 1;33(6):924-933.
- [3] Annesley CE, Brown P. Novel agents for the treatment of childhood acute leukemia. *Ther Adv Hematol*. 2015 Apr;6(2):61-79.
- [4] Stein EM, Tallman MS. Mixed lineage rearranged leukaemia: pathogenesis and targeting DOT1L. *Curr Opin Hematol*. 2015 Mar;22(2):92-6.
- [5] Yoshido A, Ishiguro K, Kitajima H, et al. DOT1L inhibition exerts the anti-tumor effect by activating interferon signaling in breast cancer cells. *Clin Epigenetics*. 2025 Nov 26;17(1):201.
- [6] Möbitz H, Machauer R, Holzer P, et al. Discovery of Potent, Selective, and Structurally Novel Dot1L Inhibitors by a Fragment Linking Approach. *ACS Med Chem Lett*. 2017 Feb 14;8(3):338-343.
- [7] Yang W, Yu H, Huang J, et al. Inhibition of Dot1L Alleviates Fulminant Hepatitis Through Myeloid-Derived Suppressor Cells. *Cell Mol Gastroenterol Hepatol*. 2021;12(1):81-98.
- [8] Kurani H, Razavipour SF, Harikumar KB, et al. DOT1L Is a Novel Cancer Stem Cell Target for Triple-Negative Breast Cancer. *Clin Cancer Res*. 2022 May 2;28(9):1948-1965.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA