

Product Data Sheet

Product Name: EPZ031686

Cat. No.: GC16224

Chemical Properties

Cas. No. 1808011-22-4

Chemical Name 6-chloro-2-oxo-N-((1R,3r,5S)-8-(((1-(4,4,4-trifluorobutyl)piperidin-4-yl)methyl)sulfonyl)-8-azabicyclo[3.2.1]octan-3-yl)indoline-5-carboxamide

SMILES C1C=CC(N2)=C(CC2=O)C=C1C(N[C@@]3([H])C[C@@](N4S(CC(CC5)CCN5CCCC(F)(F)F)(=O)=O)([H])CC[C@@]4([H])C3)=O

Formula C₂₆H₃₄ClF₃N₄O₄S

M.Wt 591.09

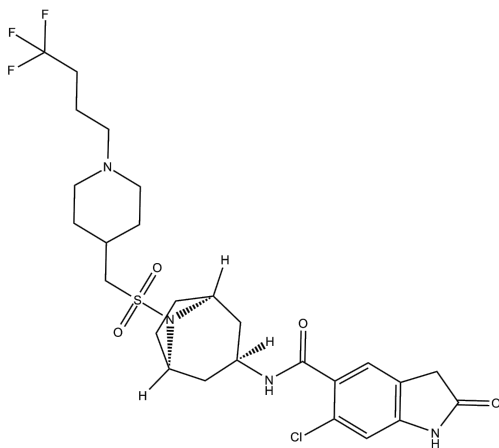
Solubility Soluble in DMSO

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]:

Cell lines HCT116 colorectal cancer cells and MDA-MB-231 breast cancer cells

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

Preparation Method Cells were cultured in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum (FBS) at 37°C, 5% CO₂. Cells were treated with EPZ031686 at concentrations ranging from 0.5μM to 50μM for 48 to 72 hours.

Reaction Conditions 0.5-50μM; 48-72h

Applications EPZ031686 significantly reduced the steady-state mRNA levels of SMYD3 target genes, including CDK2, c-MET, N-cadherin (N-CAD), and fibronectin 1 (FN1), in MDA-MB-231 cells. EPZ031686 also attenuated SMYD3-mediated ERK signaling, as evidenced by decreased ERK1/2 phosphorylation (pERK1/2) in both HCT116 and MDA-MB-231 cell lines.

Animal experiment [2]:

Animal models C57BL/6J mice

Preparation Method Mice were intraperitoneally administered EPZ031686 (20mg/kg) daily for 7 consecutive days. Mice were sacrificed and adipose tissues (iWAT, BAT, eWAT) were harvested for analysis.

Dosage form 20mg/kg; i.p.

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 EPZ031686 treatment significantly promoted white adipose tissue (WAT) browning and adaptive thermogenesis, evidenced by increased multilocular adipocytes, enhanced UCP1 protein expression, and upregulation of thermogenic genes (Ucp1, Ppargc1a, Cpt2, Cpt1a, Cpt1b) in both inguinal white adipose tissue (iWAT) and brown adipose tissue (BAT).

References:

- [1] Parenti MD, Naldi M, Manoni E, et al. Discovery of the 4-aminopiperidine-based compound EM127 for the site-specific covalent inhibition of SMYD3. *Eur J Med Chem.* 2022 Dec 5;243:114683.
- [2] Shu M, Ma Y, Zhao D, et al. Loss of histone methyltransferase Smyd3 triggers WAT browning and adaptive thermogenesis via enhancing PPAR γ expression in a H4K20me3-dependent manner. *J Transl Med.* 2025 Oct 1;23(1):1041.

Background

EPZ031686 is a potent and orally active SMYD3 inhibitor with an IC₅₀ value of 3nM. EPZ031686 noncompetitively inhibits both SAM and MEKK2, with Ki values of approximately 1.2nM and 1.1nM, respectively^[1]. By enhancing PPAR γ expression, EPZ031686 induces white adipose tissue browning and adaptive thermogenesis, offering a potential therapeutic strategy for obesity^[2]. EPZ031686 shows potential in suppressing tumor development^[3-4].

In vitro, treatment of HCT116 colorectal cancer cells and MDA-MB-231 breast cancer cells with EPZ031686 (0.5–50 μ M) for 48–72 hours significantly reduced SMYD3-mediated ERK1/2 phosphorylation and induced PARP cleavage, thereby inhibiting tumor cell proliferation and promoting apoptosis^[5].

In vivo, daily intraperitoneal administration of EPZ031686 (20mg/kg) for 7 consecutive days in mice significantly upregulated uncoupling protein 1 (UCP1) expression in inguinal white adipose tissue (iWAT) and brown adipose tissue (BAT), while activating the transcription of thermogenic genes (Ucp1, Ppargc1a, Cpt2, Cpt1a, Cpt1b), thereby promoting white fat browning and adaptive thermogenesis^[2]. A single dose of EPZ031686 (1mg/kg intravenously or 5–50mg/kg orally) in male CD-1 mice resulted in moderate clearance (27 $\pm$ 3.9mL/min/kg), a large steady-state volume of

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

distribution (2.3 ± 0.29 L/kg), and a terminal half-life of 1.7 ± 0.13 hours^[1].

References:

- [1] Mitchell LH, Boriack-Sjodin PA, Smith S, et al. Novel Oxindole Sulfonamides and Sulfamides: EPZ031686, the First Orally Bioavailable Small Molecule SMYD3 Inhibitor. ACS Med Chem Lett. 2015 Aug 27;7(2):134-8.
- [2] Shu M, Ma Y, Zhao D, et al. Loss of histone methyltransferase Smyd3 triggers WAT browning and adaptive thermogenesis via enhancing PPAR γ expression in a H4K20me3-dependent manner. J Transl Med. 2025 Oct 1;23(1):1041.
- [3] Rubio-Tomás T. Novel insights into SMYD2 and SMYD3 inhibitors: from potential anti-tumoural therapy to a variety of new applications. Mol Biol Rep. 2021 Nov;48(11):7499-7508.
- [4] Rajajeyabalachandran G, Kumar S, Murugesan T, et al. Therapeutical potential of deregulated lysine methyltransferase SMYD3 as a safe target for novel anticancer agents. Expert Opin Ther Targets. 2017 Feb;21(2):145-157.
- [5] Parenti MD, Naldi M, Manoni E, et al. Discovery of the 4-aminopiperidine-based compound EM127 for the site-specific covalent inhibition of SMYD3. Eur J Med Chem. 2022 Dec 5;243:114683.

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