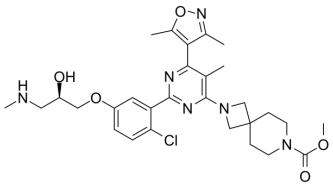
EZM 2302

Cat. No.:	HY-111109
CAS No.:	1628830-21-6
Molecular Formula:	$C_{29}H_{37}ClN_6O_5$
Molecular Weight:	585.09
Target:	Histone Methyltransferase
Pathway:	Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (170.91 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7091 mL	8.5457 mL	17.0914 mL
	5 mM	0.3418 mL	1.7091 mL	3.4183 mL
	10 mM	0.1709 mL	0.8546 mL	1.7091 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.27 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.56 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.56 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

EZM 2302 is an inhibitor of coactivator-associated arginine methyltransferase 1 (CARM1) with an IC_{50} of 6 nM.

IC_{50} & Target

IC50: 6 nM (CARM1)[1]

In Vitro

EZM 2302 binds to CARM1 and is a selective inhibitor of CARM1 activity (IC_{50}=6 nM) with broad selectivity against other histone methyltransferases. Treatment of MM cell lines with EZM 2302 leads to inhibition of PABP1 and SMB methylation and cell stasis with IC_{50} values in the nanomolar range (9, 31 nM, respectively). EZM 2302 inhibits the in vitro proliferation of

	multiple hematopoietic cell lines, with day 14 IC_{50} values of less than 100 nM in 9 of 15 cell lines[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	EZM 2302 is stable in human hepatocytes (CL<3 mL/min/kg), and moderately binds to human, mouse and rat plasma proteins with a mean fraction unbound of 0.66, 0.46 and 0.74, respectively. In mouse and rat, the plasma clearance (CL) is 43 and 91 mL/min/kg, respectively. EZM 2302 shows dose-dependent exposure and tumor growth inhibition (TGI) after 21 days in the RPMI-8226 xenograft model. Tumors in all EZM 2302 dose groups measured on day 21 show significant decreases in tumor growth compared to vehicle[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cultured cells in linear/log phase growth are split to a seeding density of 2e5 cells/mL in 2–20mLs of media, depending on the yield required at the end of the growth period. EZM 2302 is diluted in DMSO and added to each culture vessel with a final DMSO concentration of 0.2%. Cells are allowed to grow for 96 hours. At the conclusion of each treatment period, cells are harvested by centrifugation (5 minutes, 1200 rpm), and cell pellets are rinsed once with PBS before being frozen on dry ice pending further processing[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats[1] Male Sprague-Dawley rats (n=3) are treated with a single dose of EZM2302 at 2 mg/kg by intravenous (i.v.) injection and 10 mg/kg by oral gavage administration (p.o.; mouse only), formulated in 5% dextrose in water, pH 3.5. An additional group of rats, cannulated in both the jugular and portal veins are dosed by oral gavage (10 mg/kg, in 0.5% methylcellulose in water). Approximately 110 µL of blood is taken from the animals by retro-orbital bleeding (mouse), tail vein (rat i.v.) or both jugular and portal vein sampling (rat p.o.) at pre-specified time intervals. The 2 h samples are split for parallel determination of blood and plasma concentration[1]. Mice[1] RPMI-8226 cells are inoculated at 5×10^6 cells/mouse and treatment began when the mean tumor sizes reach 120 mm^3 (28 days post-inoculation). CB-17 SCID Mice are assigned into groups using a randomized block design. EZM2302 or vehicle (0.5% methylcellulose in water) is administered orally BID at a dose volume of 37.5, 75, 150, or 300 mg/kg for 21 days. Body weights are measured twice a week for the duration of the study. Tumor size is measured twice weekly in two dimensions using a caliper, and the volume is expressed in cubic millimeters. Animals are euthanized 3 hours post-final dose, with blood and tissues collected for analysis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2020 Dec 8;11(1):6297.
- Sci Adv. 2022 Dec 9;8(49):eadd8928.
- Aging (Albany NY). 2020 Jun 2;12(11):10578-10593.
- Mol Carcinog. 2023 May 5.
- Exp Cell Res. 2023 Apr 6;113586.

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REFERENCES

[1]. Drew AE, et al. Identification of a CARM1 Inhibitor with Potent In Vitro and In Vivo Activity in Preclinical Models of Multiple Myeloma. Sci Rep. 2017 Dec 21;7(1):17993.

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