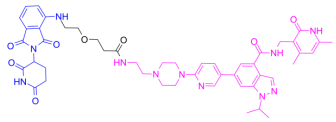
MS177

Cat. No.:	HY-148333
CAS No.:	2225938-86-1
Molecular Formula:	$C_{48}H_{55}N_{11}O_8$
Molecular Weight:	914.02
Target:	PROTACs; Histone Methyltransferase; Apoptosis
Pathway:	PROTAC; Epigenetics; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (136.76 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.0941 mL	5.4703 mL	10.9407 mL
5 mM	0.2188 mL	1.0941 mL	2.1881 mL
10 mM	0.1094 mL	0.5470 mL	1.0941 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: 2.08 mg/mL (2.28 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

MS177 is an effective and fast-acting EZH2 degrader. MS177 is a PROTAC that consists of a CRBN ligand, linker, and a potent enzymatic EZH2 inhibitor C24 (C24 IC_{50}): 12 nM). MS177 effectively depletes both canonical EZH2–PRC2 and noncanonical EZH2–cMyc complexes. MS177 induces leukaemia cell growth inhibition, apoptosis and cell cycle progression arrest[1].

IC_{50} & Target

EZH2

In Vitro

MS177 inhibits the enzymatic activities of EZH2-PRC2 (IC_{50}: 7 nM)[1].
MS177 (5 μM, 24 h) decreases H3K27me3 and increases H3K27activity in HeLa cells[1].
MS177 (0.1-5 μM, 16 h) effectively degrades cellular EZH2-PRC2 and suppresses global H3K27me3 in EOL-1 cells[1].
MS177 (0.1-5 μM, 16 h) induces Myc degradation in EOL-1 and MV4 cells[1].
MS177 (4 days) shows antiproliferation effects in a panel of MLL-r leukaemia cells and samples from patients with AML, with IC_{50}s below 2 μM[1].

MS177 (0.5-2.5 μM, 24 h) decreases colony-forming capabilities in MV4;11 cells[1].
MS177 (0.5-2.5 μM, 24 h) slows cell cycle progression and induces MOLM-13 cell apoptosis[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	AML cell line: MV4;11, MOML-13, RS4;11, KOPN-8 THP-1, EOL-1 (MLL-r cells) Control cell line: K562 (CML cells) Patient sample: AML cells
Concentration:	0-100 μM approximately
Incubation Time:	4 days
Result:	Inhibited cell proliferation with IC_{50}s of 0.1-0.57 μM for MLL-r cells, 0.09-1.35 μM for Patient sample, >100 μM for K562 cell.

Western Blot Analysis[1]

Cell Line:	EOL-1 cell
Concentration:	0.1, 0.5, 1, 2.5, 5 μM
Incubation Time:	16 h
Result:	Depleted EZH2, EED and SUZ12 in a concentration-dependent manner and suppressed global H3K27me3.

In Vivo

MS177 (100 mg/kg, i.p., BID for 6 days) represses tumor growth in PDX animal model of MLL-r AML, and in subcutaneously xenografted MLL-r leukaemia models[1].
MS177 (50 mg/kg, i.p.) achieves intraplasma concentrations about 1 μM in male Swiss Albino mice[1].
MS177 (100 mg/kg, i.p., BID for 6 days per week; and 200 mg/ kg, i.p. BID 3 days per week) is well tolerated and lacks apparent toxicity in mice[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	PDX animal model of MLL-r AML[1]
Dosage:	100 mg/kg
Administration:	Intraperitoneal injection (i.p.), BID for 6 days.
Result:	Inhibited tumor growth and prolonged survival.

REFERENCES

[1]. Wang J, et al. EZH2 noncanonically binds cMyc and p300 through a cryptic transactivation domain to mediate gene activation and promote oncogenesis. Nat Cell Biol. 2022 Mar;24(3):384-399.

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