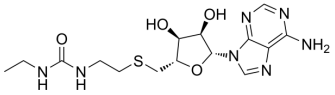
DS-437

Cat. No.:	HY-124131
CAS No.:	1674364-87-4
Molecular Formula:	$C_{15}H_{23}N_7O_4S$
Molecular Weight:	397.45
Target:	Histone Methyltransferase
Pathway:	Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (314.50 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5160 mL	12.5802 mL	25.1604 mL
	5 mM	0.5032 mL	2.5160 mL	5.0321 mL
	10 mM	0.2516 mL	1.2580 mL	2.5160 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 (5.23 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.23 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.23 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

DS-437 is a dual PRMT5/7 inhibitor (IC_{50}s of PRMT5/7=6 μM). DS-437 is selective for PRMT5 and PRMT7 over 29 other human protein-, DNA-, and RNA-methyltransferases. DS-437 is a S-adenosylmethionine (SAM)-competitive inhibitor of PRMT5. DS-437 also inhibits DNMT3A and DNMT3B, with IC_{50}s of 52 and 62 μM, respectively. DS-437 inhibits the methylation of FOXP3[1] [2].

IC_{50} & Target	PRMT5	PRMT7

In Vitro	DS-437 was able to inhibit methylation of an H4[1–24] peptide by the PRMT5–MEP50 complex under balanced conditions (cofactor and substrate concentrations set at their respective?Km?values) in a dose-dependent manner with an IC_{50}?of 5.9 ± 1.4 μM[1]. ?DS-437 increased total $CD8^+$?and $CD8^+$ $PD\text{-}1^+$ T cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

DS-437 (10 mg/kg; i.p.; 5 times a week) has some beneficial effects on inhibiting tumor growth. The combination of DS-437 and the anti-$p185^{erbB2/neu}$?antibody 4D5 had even more dramatic effects[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Six to Ten weeks old female Balb/c mice (bearing CT26Her2 tumor cells)[1]
Dosage:	10 mg/kg
Administration:	i.p.; 5 times a week
Result:	Had some beneficial effects on inhibiting tumor growth.

REFERENCES

[1]. Smil D, et al. Discovery of a Dual PRMT5-PRMT7 Inhibitor.ACS Med Chem Lett. 2015 Mar 2;6(4):408-12.

[2]. Nagai Y, et al. PRMT5 Associates With the FOXP3 Homomer and When Disabled Enhances Targetedp185erbB2/neu Tumor Immunotherapy.Front Immunol. 2019 Feb 8;10:174.

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