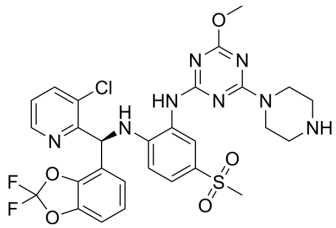
Dot1L-IN-4

Cat. No.:	HY-135127
CAS No.:	2565705-02-2
Molecular Formula:	$C_{28}H_{27}ClF_2N_8O_5S$
Molecular Weight:	661.08
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 : ≥ 220 mg/mL (332.79 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5127 mL	7.5634 mL	15.1268 mL
5 mM	0.3025 mL	1.5127 mL	3.0254 mL
10 mM	0.1513 mL	0.7563 mL	1.5127 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 (3.15 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (3.15 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.15 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Dot1L-IN-4 is a potent disruptor of telomeric silencing 1-like protein (DOT1L) inhibitor with an $IC_{50\ SPA\ DOT1L}$ of 0.11 nM[1].

IC_{50} & Target

DOT1L

0.11 nM (IC_{50})

In Vitro

Dot1L-IN-4 (Compound 10) is tested in cellular assays to assess the ability to inhibit the dimethylation of H3K79 in HeLa cells

	($ED_{50\ H3K79me2\ Elisa}$=1.7 nM) and HOXA9 gene expression in Molm-13 cells ($ED_{50\ HOXA9\ RGA}$=33 nM). Dot1L-IN-4 also inhibits mixed lineage leukemia (MLL) with an IC_{50} of 99 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Dot1L-IN-4 (Compound 10; 300 mg/kg; p.o.; qd) is not tolerated at such a high dose by tumor xenograft bearing mice, and at a 6-fold reduced dose, the tumor growth as well as the HOXA9 reporter gene mRNA are reduced only by less than half as compared to control animals[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male mice (C57BL/6) bearing subcutaneous MV4-11 tumor xenografts[1]
Dosage:	300 mg/kg (Pharmacokinetic Analysis)
Administration:	P.o.
Result:	Was not tolerated at such a high dose by tumor xenograft bearing mice, and at a 6-fold reduced dose, the tumor growth as well as the HOXA9 reporter gene mRNA were reduced only by less than half as compared to control animals.

REFERENCES

[1]. Frédéric Stauffer, et al. New Potent DOT1L Inhibitors for in Vivo Evaluation in Mouse. ACS Med. Chem. Lett. 2019, 10, 12, 1655-1660.

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