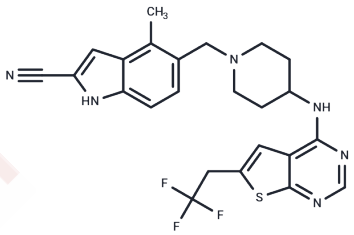
Data Sheet (Cat.No.TQ0058)

TargetMol

MI-463

Chemical Properties



CAS No. : 1628317-18-9

Formula: C24H23F3N6S

Molecular Weight: 484.54

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	MI-463 is a potent and orally bioavailable inhibitor of the menin-mLL interaction (IC50: 15.3 nM).
Targets(IC50)	Epigenetic Reader Domain,Histone Methyltransferase
In vitro	Treatment of murine bone marrow cells (BMC) transformed with the mLL-AF9 oncogene with MI-463 results in substantial growth inhibition (GI50: 0.23 μM). MI-463 is effective in inducing differentiation of MLL leukemia cells. Treatment with sub-micromolar concentrations of MI-463 also leads to markedly reduced expression of Hoxa9 and Meis1.
In vivo	MI-463 shows substantial survival benefit in mouse models of MLL leukemia. It has very favorable druglike properties, including metabolic stability and PK profile in mice. MI-463 achieves high level in peripheral blood following a single intravenous or oral dose, while also showing high oral bioavailability (45%). MI-463 induces strong inhibition of tumor growth with once-daily intraperitoneal (i.p.) administration. The expression of mLL fusion protein target genes, HOXA9 and MEIS1, is significantly reduced upon treatment with MI-463.
Cell Research	Leukemia cells are treated with MI-463 or 0.25% DMSO and cultured at 37 °C for 7 days. Media is changed on day 4, viable cell numbers are restored to the original concentration and MI-463 is re-supplied. MTT cell proliferation assay kit is then employed, and plates are read for absorbance at 570 nm using a microplate reader.
Animal Research	For efficacy studies in MV4;11 subcutaneous xenograft mice model, 5×10^6 cells are injected into the 4-6 week old female BALB/c nude mice. Treatment is started when the tumor size reached ~100 mm^3. Vehicle (25% DMSO, 25% PEG400, 50% PBS) or MI-463 are administrated once daily at designated doses using i.p. injections.

Solubility Information

Solubility	DMSO: 120 mg/mL (247.66 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4 mg/mL (8.26 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one.*

In vivo Formulation	*Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0638 mL	10.3191 mL	20.6381 mL
5 mM	0.4128 mL	2.0638 mL	4.1276 mL
10 mM	0.2064 mL	1.0319 mL	2.0638 mL
50 mM	0.0413 mL	0.2064 mL	0.4128 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Borkin D, et al. Pharmacologic inhibition of the Menin-MLL interaction blocks progression of MLL leukemia in vivo. Cancer Cell. 2015 Apr 13;27(4):589-602.