产品名称：**MI-463**
产品别名：**MI-463**

生物活性：

Description	MI-463 is a highly potent and orally bioavailable small molecule inhibitor of the menin-mLL interaction.
In Vitro	MI-463 can reach the target protein in mammalian cells and effectively inhibit the menin-mLL-AF9 interaction at sub-micromolar concentrations. Treatment of murine bone marrow cells (BMC) transformed with the mLL-AF9 oncogene with MI-463 results in substantial growth inhibition, with GI50 of 0.23 μM[1].
In Vivo	MI-463 achieves high level in peripheral blood following a single intravenous or oral dose, while also showing high oral bioavailability (45%). Pharmacologic inhibition of the menin-mLL interaction substantially delays progression of mLL leukemia in murine models through on-target activity without causing toxicity. 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, are significant reduced upon treatment with MI-463. 20 days treatment of MV4;11 xenograft recipient mice with MI-463 also results in a substantial delay in leukemia progression as manifested by a marked decrease in the bioluminescence level which is associated with a significant decrease in the population of leukemic cells in the peripheral blood, spleen and bone marrow samples[1].

Solvent&Solubility

In Vitro:

DMSO : 125 mg/mL (**257.98 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.08 mg/mL (4.29 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (4.29 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

Solubility: 2.08 mg/mL (4.29 mM); Suspended solution; Need ultrasonic

此方案可获得 2.08 mg/mL (4.29 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

	以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.08 mg/mL (4.29 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.29 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. 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.

实验参考：

Cell Assay	Leukemia cells are treated with MI-463 or 0.25% DMSO and cultured at 37 °C for 7 days. Media is changed at day 4, viable cell numbers are restored to the original concentration and MI-463 are re-supplied. MTT cell proliferation assay kit is then employed, and plates are read for absorbance at 570 nm using a microplate reader[1].
Animal Administration	Mice: 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 compounds (MI-463 or MI-503) are administrated once daily at designated doses using i.p. injections[1].
References	[1]. 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.