产品名称：MI-503
产品别名：MI-503

生物活性：

Description	MI-503 is a highly potent and orally bioavailable small molecule inhibitor of the menin-mLL interaction.
In Vitro	MI-503 occupies the F9 and P13 pockets on menin, forming a hydrogen bond with Tyr276, and also extends beyond the P13 pocket to form hydrogen bonds with Trp341 and Glu366. Treatment of murine bone marrow cells (BMC) transformed with the mLL-AF9 oncogene with MI-503 results in substantial growth inhibition, with GI50 of 0.22 μM. The cell growth inhibitory effect of MI-503 is time-dependent, with a pronounced effect achieved after 7-10 days of treatment[1].
In Vivo	MI-503 achieves high level in peripheral blood following a single intravenous or oral dose, while also showing high oral bioavailability (75%). MI-503 induces strong inhibition of tumor growth with once daily intraperitoneal (i.p.) administration. Treatment with MI-503 results in an over 80% reduction in MV4;11 tumor volume and complete tumor regression in two mice. Ten consecutive days of treatment with MI-503 results in a marked delay in progression of mLL leukemia in mice and significantly reduces leukemia tumor burden. Treatment with MI-503 and MI-463 leads to markedly reduced expression of Hoxa9 and Meis1, downstream targets of mLL fusion proteins substantially upregulated in mLL leukemias[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 25 mg/mL** (**44.28 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	1.7711 mL	8.8554 mL	17.7107 mL
	5 mM	0.3542 mL	1.7711 mL	3.5421 mL
	10 mM	0.1771 mL	0.8855 mL	1.7711 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 (3.68 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (3.68 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 (3.68 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (3.68 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 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 (3.68 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (3.68 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-503 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-503 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.