产品名称：SAR405838
产品别名：SAR405838

生物活性：

Description

SAR405838 is a highly potent and selective MDM2 inhibitor, binds to MDM2 with Ki= 0.88 nM and has high specificity over other proteins. IC50 value: 0.88 nM (Ki) [1] Target: MDM2 in vitro: SAR405838 potently inhibits cell growth in cancer cell lines, including SJSA-1 (IC50, 0.092 μM), RS4;11 (IC50, 0.089 μM), LNCaP (IC50, 0.27 μM), and HCT-116 (IC50, 0.20 μM) cells, and displays high selectivity over cancer cell lines with mutated or deleted p53, including SAOS-2 (IC50, >10 μM), PC-3 (IC50, >10 μM), SW620 (IC50, >10 μM), and HCT-116 (p53-/-) (IC50, >20 μM) cells.[1] SAR405838 effectively induces apoptosis in the RS4;11 cell line. SAR405838 potently inhibits cell growth and induces dose-dependent apoptosis in the ABTR1 and ABTR2 sublines, albeit with modestly reduced potency compared with that in the control RS4;11 cell line.[2] in vivo: At well-tolerated dose schedules, SAR405838 achieves either durable tumor regression or complete tumor growth inhibition in mouse xenograft models of SJSA-1 osteosarcoma, RS4;11 acute leukemia, LNCaP prostate cancer and HCT-116 colon cancer. Remarkably, a single oral dose of SAR405838 is sufficient to achieve complete tumor regression in the SJSA-1 model. In the SJSA-1 osteosarcoma, acute lymphoblastic leukemia RS4;11, LNCaP prostate cancer, and HCT-116 colon cancer xenograft model, MI-773 (p.o.) effectively inhibits tumor growth in a dose-dependent manner (10 mg/kg, 30 mg/kg, 50 mg/kg, 100 mg/kg, and 200 mg/kg,). [1]

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (**88.89 mM**)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7778 mL	8.8889 mL	17.7778 mL
5 mM	0.3556 mL	1.7778 mL	3.5556 mL
10 mM	0.1778 mL	0.8889 mL	1.7778 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: ≥ 2.5 mg/mL (4.44 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.44 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 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% corn oil Solubility: ≥ 2.5 mg/mL (4.44 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.44 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Wang S, et al. SAR405838: an optimized inhibitor of MDM2-p53 interaction that induces complete and durable tumor regression. Cancer Res. 2014 Oct 15;74(20):5855-5865. [2]. Hoffman-Luca CG, et al. Elucidation of Acquired Resistance to Bcl-2 and MDM2 Inhibitors in Acute Leukemia In Vitro and In Vivo. Clin Cancer Res. 2015 Jun 1;21(11):2558-2568.