产品名称：**DMH 1**
产品别名：**DMH-1**

生物活性：

Description	DMH-1 is a potent and selective **BMP** inhibitor with **IC_{50}**s of 27/107.9/<5/47.6 nM for ALK1/ALK2/ALK3/ALK6, respectively.
IC_{50} & Target	IC50: 27 nM (ALK1), 107.9 nM (ALK2), <5 nM (ALK3), 47.6 nM (ALK6)[1]
In Vitro	DMH-1 (0.5 μM) induces regulation of OCT4, Nanog, and PAX6 protein expression. DMH-1 significantly reduces the percentage of cells expressing the pluripotency marker proteins OCT4 and Nanog in both SM3 and CA6 cells. PAX6 expression is significantly up-regulated by day 5 and day 7 in CA6 and SM3 cells, respectively. DMH-1 induces regulation of pluripotency and neural precursor marker mRNAs. PAX6 can regulate the expression of SOX1 independently by manipulating the DMH-1 concentration during the neural induction of hiPSCs[2]. DMH-1 (5 μM and 10 μM) inhibits CDDP-induced autophagy in HeLa cells and enhances the ability of CDDP to reduce HeLa cell viability, inhibits tamoxifen-induced autophagy in MCF-7 cells and enhances the ability of tamoxifen to reduce MCF-7 cell viability, inhibits 5-FU-induced autophagy in both MCF-7 and HeLa cells but does not affect the inhibitory effects of 5-FU on MCF-7 and HeLa cell viability. DMH-1 enhances the apoptotic induction effects of CDDP on HeLa cells after 24 h treatment. DMH-1 inhibits HeLa and MCF-7 cell proliferation[3]. DMH-1 (20 μM) reduces the canonical phosphorylation of Smads 1,5 and 9. DMH-1 in combination with Cisplatin significantly decreases Ki-67 positive staining in the OVCAR8 cells. DMH-1 (20 μM) upregulates JAG1, reduces CYP1B1 and increases HAPLN1 expression in both OVCAR8 and NCI-RES cells[4].
In Vivo	DMH1 (5 mg/kg, i.p.) treatment significantly reduces the tumor growth in human lung cancer xenograft model[5].

Solvent&Solubility

In Vitro:

DMSO : 11.5 mg/mL (30.23 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6285 mL	13.1427 mL	26.2854 mL
	5 mM	0.5257 mL	2.6285 mL	5.2571 mL
	10 mM	0.2629 mL	1.3143 mL	2.6285 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: ≥ 1 mg/mL (2.63 mM); Clear solution

此方案可获得 ≥ 1 mg/mL (2.63 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 10.0 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。
References	[1]. Engers DW, et al. Synthesis and structure-activity relationships of a novel and selective bone morphogenetic protein receptor (BMP) inhibitor derived from the pyrazolo[1.5-a]pyrimidine scaffold of dorsomorphin: the discovery of mL347 as an ALK2 versus ALK3 selective mLPCN probe. Bioorg Med Chem Lett. 2013 Jun 1;23(11):3248-52. [2]. Sheng Y, et al. DMH1 (4-[6-(4-isopropoxyphenyl)pyrazolo[1,5-a]pyrimidin-3-yl]quinoline) inhibits chemotherapeutic drug-induced autophagy. Acta Pharm Sin B. 2015 Jul;5(4):330-6. [3]. Neely MD, et al. DMH1, a highly selective small molecule BMP inhibitor promotes neurogenesis of hiPSCs: comparison of PAX6 and SOX1 expression during neural induction. ACS Chem Neurosci. 2012 Jun 20;3(6):482-91. [4]. Hover LD, et al. Small molecule inhibitor of the bone morphogenetic protein pathway DMH1 reduces ovarian cancer cell growth. Cancer Lett. 2015 Nov 1;368(1):79-87. [5]. Hao J, et al. DMH1, a small molecule inhibitor of BMP type i receptors, suppresses growth and invasion of lung cancer. PLoS One. 2014 Mar 6;9(6):e90748.

实验参考：

Cell Assay	Cells are seeded in 96-well plates and treated with different drugs for appropriate time. Then 5 mg/mL MTT is added and incubated for 4 h at 37°C. Medium is then removed and 200 μL of DMSO is added to dissolve the crystal. Absorbance is measured at a wavelength of 490 nm with a plate reader. [3]
Animal Administration	Sub-confluent A549 cells are trypsinized and then suspended in serum free RPMI 1640 medium. The cell suspension (1×10^6 cells in 100 μL medium for each injection) is injected subcutaneously into both the right and left flanks of eight-week old NOD SCID mice (n=5 for each group). Mice are given Intraperitoneal (i.p.) injection of the vehicle (12.5% 2-hydroxypropyl-β-cyclodextrin) or 5 mg/kg DMH1 every other day. The tumor sizes are measured with a vernier caliper from the sixth day to the fourth week after tumor implantation. The tumor volume (V) is calculated according to the formulation: Volume=$(\text{width})^2\times\text{length}/2$. The tumor tissues are dissected at the end of study, and are sectioned and stained with H & E, and for immunohistochemical analysis. [5]
References	[1]. Engers DW, et al. Synthesis and structure-activity relationships of a novel and selective bone morphogenetic protein receptor (BMP) inhibitor derived from the pyrazolo[1.5-a]pyrimidine scaffold of dorsomorphin: the discovery of mL347 as an ALK2 versus ALK3 selective mLPCN probe. Bioorg Med Chem Lett. 2013 Jun 1;23(11):3248-52. [2]. Sheng Y, et al. DMH1 (4-[6-(4-isopropoxyphenyl)pyrazolo[1,5-a]pyrimidin-3-yl]quinoline) inhibits chemotherapeutic drug-induced autophagy. Acta Pharm Sin B. 2015 Jul;5(4):330-6. [3]. Neely MD, et al. DMH1, a highly selective small molecule BMP inhibitor promotes neurogenesis of hiPSCs: comparison of PAX6 and SOX1 expression during neural induction. ACS Chem Neurosci. 2012 Jun 20;3(6):482-91. [4]. Hover LD, et al. Small molecule inhibitor of the bone morphogenetic protein pathway DMH1 reduces ovarian cancer cell growth. Cancer Lett. 2015 Nov 1;368(1):79-87. [5]. Hao J, et al. DMH1, a small molecule inhibitor of BMP type i receptors, suppresses growth and invasion of lung cancer. PLoS One. 2014 Mar 6;9(6):e90748.