上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：S63845
产品别名：S63845

生物活性：

Description	S63845 is a potent and selective myeloid cell leukemia 1 (MCL1) inhibitor with a K_d of 0.19 nM for human MCL1.
IC_{50} & Target	MCL1
	0.19 nM (Kd)
In Vitro	The pro-survival protein myeloid cell leukemia 1 (MCL1) is over expressed in many cancers. S63845 is a small molecule that specifically binds with high affinity to the BH3-binding groove of MCL1. S63845 potently kills MCL1-dependent cancer cells, including multiple myeloma, leukaemia and lymphoma cells, by activating the BAX/BAK-dependent mitochondrial apoptotic pathway. The activity of S63845 is next evaluated in a panel of eight AML cell lines: all lines are sensitive to S63845 (IC_{50}=4-233 nM)[1].
In Vivo	S63845 shows potent anti-tumour activity with an acceptable safety margin as a single agent in several cancers. Intravenously injected (i.v.) S63845 exerts dose-dependent anti-tumour activity in human multiple myeloma (H929 and AMO1) xenografts in immunocompromised mice, with maximal tumour growth inhibition of 114% in the AMO1 model and 103% in the H929 model. At 25 mg/kg, S63845 induces complete regression in 7 out of 8 of the mice at 100 days after treatment in the AMO1 model[1].
Solvent&Solubility	***In Vitro:***
	DMSO : 33.33 mg/mL (40.19 mM; Need ultrasonic)
	H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.2059 mL	6.0295 mL	12.0589 mL
	5 mM	0.2412 mL	1.2059 mL	2.4118 mL
	10 mM	0.1206 mL	0.6029 mL	1.2059 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 (2.51 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (2.51 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 (2.51 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (2.51 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。
References	[1]. Kotschy A, et al. The MCL1 inhibitor S63845 is tolerable and effective in diverse cancer models. Nature. 2016 Oct 27;538(7626):477-482.

实验参考：

Cell Assay	Cells are treated with increasing doses of S63845 (typically 0.008, 0.025, 0.04, 0.2, 1, 5 μM) for 24 h. Cells are stained with Annexin V-FITC and propidium iodide, analysed on a FACS Calibur and live cells are recorded. Data are presented as per cent cell death induction relative to cells cultured in medium alone[1].
Animal Administration	Mice: S63845 is formulated extemporaneously in 25 mM HCl, 20% 2-hydroxy propyl β -cyclo dextrin 20% and administrated at the 6.25, 12.5, 25 mg/kg for 0, 20, 40, 60, 80 days. Tumour growth inhibition (TGImax) is calculated[1].
Kinase Assay	10 mM HEPES pH 7.4, 175 mM NaCl, 25 μM EDTA, 1 mM TCEP, 0.01% P20 and 1% DMSO is used as a running buffer. The ligand surface is generated using double His-tagged proteins. Serial dilutions of the compound in buffer are injected over the protein surface. All sample measurements are performed at a flow rate of 30 μL per min (injection time 120 s, dissociation time 360 s). The sensor surface is regenerated by consecutive injections of 0.35 M EDTA pH 8.0 with 0.1 mg/mL trypsin, 0.5 M imidazole and 45% DMSO (60 s, 15 μL per min)[1].
References	[1]. Kotschy A, et al. The MCL1 inhibitor S63845 is tolerable and effective in diverse cancer models. Nature. 2016 Oct 27;538(7626):477-482.