产品名称：SP2509
产品别名：SP2509

生物活性：

Description	SP2509 is a potent and selective antagonist of lysine specific demethylase 1 (LSD1) with IC50 of 13 nM.
IC_{50} & Target	IC50: 13 nM (LSD1)[1]
In Vitro	SP2509 (250, 500, 1000 nM) inhibits LSD1 activity, depletes colony growth and induces apoptosis and cell death of cultured human acute myeloid leukemia cells, and increases H3K4Me3 on the promoters of p57 Kip, KLF4, and p21 and induces mRNA expression of p57Kip, KLF4 and p21 in AML cells. SP2509 (250, 1000 nM) induces features of morphologic differentiation of cultured and primary AML cells. Besides, SP2509 in combination with PS exerts synergistic lethal activity against cultured and primary AML cells[1]. SP2509 does not destabilize the CoREST-LSD1 interaction, and has no major destabilizing effect on the CRC. SP2509 (1 or 10 μM) induces cell death, but there are no morphological changes at a low concertation of 0.1 μM. SP2509 likewise interferes with the viability of medulloblastoma cells[2].
In Vivo	Treatment with SP2509 (25 mg/kg) and/or PS (5 mg/kg) significantly enhances PS-mediated loss of viability of $CD34^+$ primary AML cells and improves the survival of mice bearing AML xenografts and primagrafts[2].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 33 mg/mL (75.36 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	2.2836 mL	11.4181 mL	22.8363 mL
	5 mM	0.4567 mL	2.2836 mL	4.5673 mL
	10 mM	0.2284 mL	1.1418 mL	2.2836 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 (4.75 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (4.75 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。

[1]. Fiskus W, et al. Highly effective combination of LSD1 (KDM1A) antagonist and pan-histone

References	deacetylase inhibitor against human AML cells. Leukemia. 2014 Nov;28(11):2155-64. [2]. Inui K, et al. Stepwise assembly of functional C-terminal REST/NRSF transcriptional repressor complexes as a drug target. Protein Sci. 2017 Feb 20

实验参考：

Cell Assay	Daoy and D283 Med cells are used in the assay. ONS-76 cells used. All medulloblastoma cell lines are kept in an incubator at 37°C in a 5% CO_2/5% O_2/90% N_2 atmosphere with maximum humidity. XTT assays are performed in triplicates (n = 3) with three replicates for each using 1×10^3 Daoy cells/well, 4×10^3 D283 Med cells/well, and 1×10^3ONS-76 cells/well in 100 µL of medium at initial seeding in 96-well plates. [2]
Animal Administration	Female NOD/SCID mice are exposed to 2.5 Gy of radiation. The following day, 5 million OCI-AmL3 cells are injected into the lateral tail vein of the mice and the mice are monitored for 7 days. Following treatments are administered in cohorts of 8 mice for each treatment: vehicle alone, 25 mg/kg SP2509, 5 mg/kg LBH589 and SP2509 plus LBH589. Treatments are initiated on day 7 for OCI-AmL3 cells. SP2509 (formulated in solubilization buffer [20% Cremaphor, 20% DMSO, 60% sterile water]) is administered twice per week (Tues and Thurs) intraperitoneally (IP) for 3 weeks, and then discontinued. LBH589 (formulated in 5% DMSO/ 95% normal saline) is administered by IP injection 3 days per week (M-W-F) for 3 weeks and discontinued. The doses of PS utilized in these studies are determined to be safe and effective. A separate in vivo experiment is conducted utilizing NSG mice and primary AmL cells. Following engraftment of the AmL cells (presence of greater than 1% $CD45^+$ cells in the peripheral blood), mice are treated with SP2509 and/or PS, for three weeks. [1]
References	[1]. Fiskus W, et al. Highly effective combination of LSD1 (KDM1A) antagonist and pan-histone deacetylase inhibitor against human AML cells. Leukemia. 2014 Nov;28(11):2155-64. [2]. Inui K, et al. Stepwise assembly of functional C-terminal REST/NRSF transcriptional repressor complexes as a drug target. Protein Sci. 2017 Feb 20