产品名称：**LMK 235**
产品别名：**LMK-235**

生物活性：

Description

LMK-235 is a potent and selective **HDAC4/5** inhibitor, inhibits HDAC5, HDAC4, HDAC6, HDAC1, HDAC2, HDAC11 and HDAC8, with **IC_{50}**s of 4.22 nM, 11.9 nM, 55.7 nM, 320 nM, 881 nM, 852 nM and 1278 nM, respectively, and is used in cancer research.

IC_{50} & Target

HDAC5	HDAC4	HDAC6	HDAC1	HDAC11
4.22 nM (IC_{50})	11.9 nM (IC_{50})	55.7 nM (IC_{50})	320 nM (IC_{50})	852 nM (IC_{50})
HDAC2	HDAC8			
881 nM (IC_{50})	1278 nM (IC_{50})			

In Vitro

LMK-235 shows cytotoxic activity against human ovarian cancer cell lines A2780 and A2780 CisR, with IC50s of 0.49 μM and 0.32 μM, respectively. LMK-235 inhibits HDAC in A2780 and A2780 CisR cell lines, with IC50s of 0.65 μM and 0.32 μM, respectively. LMK-235 produces a higher reduction in cell viability in comparison to the combination of cisplatin and vorinostat in all cell lines[1]. LMK-235 (0, 0.625, 1.25, 2.5, 5, 10, and 20 μM) reduces the proliferation of BC cells in a dose- and time-dependent manner. LMK-235 (0-800 nM) also inhibits the growth of BC cells. Moreover, LMK-235 synergizes with bortezomib in BC cell lines[2]. LMK235 (2, 20 nM) decreases in HDAC4 nuclear accumulation in Cdkl5 -/Y NPCs, completely restores the reduced number of neurons generated from Cdkl5 -/Y NPCs. LMK235 also restores histone 3 acetylation in Cdkl5 -/Y NPCs. LMK235 causes a notable increase in the isoform IV, but does not affect BDNF isoforms I or II[3].

In Vivo

LMK235 (5 and 20 mg/kg) restores survival and maturation of postmitotic granule neurons in Cdkl5 -/Y mice. LMK235 also restores synapse development in the dentate gyrus and hippocampus of Cdkl5 -/Y mice. Furthermore, LMK235 restores hippocampus-dependent learning and memory in Cdkl5 -/Y mice[3].

Solvent&Solubility

In Vitro:

DMSO : ≥ 30 mg/mL (101.92 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.3973 mL	16.9866 mL	33.9732 mL
	5 mM	0.6795 mL	3.3973 mL	6.7946 mL
	10 mM	0.3397 mL	1.6987 mL	3.3973 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 (8.49 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.49 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% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (8.49 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.49 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 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: ≥ 2.5 mg/mL (8.49 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.49 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]. Marek L, et al. Histone deacetylase (HDAC) inhibitors with a novel connecting unit linker region reveal a selectivity profile for HDAC4 and HDAC5 with improved activity against chemoresistant cancer cells. J Med Chem. 2013 Jan 24;56(2):427-36. [2]. Li A, et al. HDAC5, a potential therapeutic target and prognostic biomarker, promotes proliferation, invasion and migration in human breast cancer. Oncotarget. 2016 Jun 21;7(25):37966-37978. [3]. Trazzi S, et al. HDAC4: a key factor underlying brain developmental alterations in CDKL5 disorder. Hum Mol Genet. 2016 Sep 15;25(18):3887-3907.

实验参考：

Cell Assay	The rate of cell survival under the action of test substances is evaluated by an improved MTT assay. The assay is based on the ability of viable cells to metabolize yellow 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) to violet formazan that can be detected spectrophotometrically. In brief, A2780, Cal27, Kyse510, and MDA-MB-231 cell lines are seeded at a density of 5000, 7000, 8000, and 10 000 cells/well in 96-well plates. After 24 h, cells are exposed to increased concentrations of the test compounds. Incubation is ended after 72 h, and cell survival is determined by addition of MTT solution (5 mg/mL in phosphate buffered saline). The formazan precipitate is dissolved in DMSO. Absorbance is measured at 544 and 690 nm in a FLUOstar microplate reader[1].
References	[1]. Marek L, et al. Histone deacetylase (HDAC) inhibitors with a novel connecting unit linker region reveal a selectivity profile for HDAC4 and HDAC5 with improved activity against chemoresistant cancer cells. J Med Chem. 2013 Jan 24;56(2):427-36. [2]. Li A, et al. HDAC5, a potential therapeutic target and prognostic biomarker, promotes proliferation, invasion and migration in human breast cancer. Oncotarget. 2016 Jun 21;7(25):37966-37978. [3]. Trazzi S, et al. HDAC4: a key factor underlying brain developmental alterations in CDKL5 disorder. Hum Mol Genet. 2016 Sep 15;25(18):3887-3907.