产品名称：**TMP269**
产品别名：**TMP269**

生物活性：

Description

TMP269 is a novel and selective class IIa **histone deacetylase (HDAC)** inhibitor with **IC_{50}**s of 157 nM, 97 nM, 43 nM and 23 nM for HDAC4, HDAC5, HDAC7 and HDAC9, respectively.

IC_{50} & Target

HDAC9	HDAC7	HDAC5	HDAC4	HDAC8
23 nM (IC_{50})	43 nM (IC_{50})	97 nM (IC_{50})	157 nM (IC_{50})	42000 nM (IC_{50})

HDAC6
82000 nM (IC_{50})

In Vitro

TMP269 has no impact on the mitochondrial activity and/or the viability of human CD4+ T cells at 10 μM, and may be used as tools to identify the endogenous substrates of the class IIa HDAC enzymes[1]. In IEC-18 intestinal epithelial cells, TMP269 prevents cell cycle progression, DNA synthesis, and proliferation induced in response to G protein-coupled receptor/PKD1 activation[2]. As with HDAC4 knockdown, TMP269 significantly enhances cytotoxicity induced by CFZ in MM cell lines, upregulating ATF4 and CHOP and inducing apoptosis. TMP269 does not hyperacetylate histone H3K9 or α-tubulin in MM cell lines, confirming that it has no inhibitory effects on class I or IIb HDACs. In a dosedependent manner, TPM269-induced cytotoxicity is associated with cleavage of caspase-8, -9, -3 and PARP, consistent with apoptosis[3].

Solvent&Solubility

In Vitro:

DMSO : ≥ 41 mg/mL (79.69 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9436 mL	9.7178 mL	19.4356 mL
	5 mM	0.3887 mL	1.9436 mL	3.8871 mL
	10 mM	0.1944 mL	0.9718 mL	1.9436 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 (4.86 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.86 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。

References	[1]. Lobera M, et al. Selective class IIa histone deacetylase inhibition via a nonchelating zinc-binding group. Nat Chem Biol. 2013 May;9(5):319-25. [2]. Sinnett-Smith J, et al. Protein kinase D1 mediates class IIa histone deacetylase phosphorylation and nuclear extrusion in intestinal epithelial cells: role in mitogenic signaling. Am J Physiol Cell Physiol. 2014 May 15;306(10):C961-71. [3]. Kikuchi S, et al. Class IIa HDAC inhibition enhances ER stress-mediated cell death in multiple myeloma. Leukemia. 2015 Sep;29(9):1918-1927.

实验参考：

Cell Assay	Human $CD4^+$ T cells are isolated from whole blood via negative selection according to manufacturer's instructions (RosetteSep Human $CD4^+$ T cell enrichment kit), re-suspended in T-cell culture medium (10% FBS, 2 mM L-glutamine, 1 mM pyruvate, 10 mM HEPES, 10 U/10 mg penicillin/streptomycin, 0.5% DMSO in RPMI) and plated at 50,000 cells/well with IL-2 (10 BRMP units/mL) and 100,000 human T-expander Dynabeads for 72 h. Determination of mitochondrial function or cell viability is done according to manufacturer's instructions (Cell Proliferation Assay Kit I (MTT)) and is represented as a percent of control (no inhibitor) wells. [1]
Kinase Assay	Dose-response studies are done with ten concentrations in a threefold dilution series from a maximum final compound concentration of 100 μM in the reaction mixture. All assays are based on the same principle as the HDAC9 assay described above: the deacetylation of acetylated or trifluoroacetylated lysine residues on fluorogenic peptide substrates by HDAC. HDAC1, HDAC2, HDAC3, HDAC6, HDAC10 and HDAC11 used a substrate based on residues 379-382 of p53 (Arg-His-Lys-Lys(Ac)). For HDAC8, the diacetylated peptide substrate, based on residues 379-382 of p53 (Arg-His-Lys(Ac)-Lys(Ac)), is used. HDAC4, HDAC5, HDAC7 and HDAC9 assays used the class IIa HDAC-specific fluorogenic substrate (Boc-Lys(trifluoroacetyl)-AMC). All reactions are done with 50 μM HDAC substrate in assay buffer (50 mM Tris-HCl, pH 8.0, 137 mM NaCl, 2.7 mM KCl, 1 mM $MgCl_2$, 1 mg/mL BSA) containing 1% DMSO final concentration; incubated for 2 h at 30°C; and developed with trichostatin A and trypsin. [1]
References	[1]. Lobera M, et al. Selective class IIa histone deacetylase inhibition via a nonchelating zinc-binding group. Nat Chem Biol. 2013 May;9(5):319-25. [2]. Sinnett-Smith J, et al. Protein kinase D1 mediates class IIa histone deacetylase phosphorylation and nuclear extrusion in intestinal epithelial cells: role in mitogenic signaling. Am J Physiol Cell Physiol. 2014 May 15;306(10):C961-71. [3]. Kikuchi S, et al. Class IIa HDAC inhibition enhances ER stress-mediated cell death in multiple myeloma. Leukemia. 2015 Sep;29(9):1918-1927.