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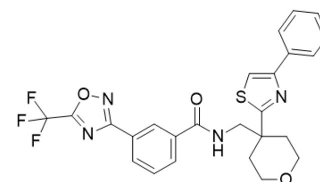
Product Data Sheet

Inhibitors • Agonists • Screening Libraries

TMP269

Cat. No.:	HY-18360
CAS No.:	1314890-29-3
Molecular Formula:	$C_{25}H_{21}F_3N_4O_3S$
Molecular Weight:	514.52
Target:	HDAC
Pathway:	Cell Cycle/DNA Damage; Epigenetics
Storage:	Powder -20°C 3 years; 4°C 2 years In solvent -80°C 6 months; -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 41 mg/mL (79.69 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.86 mM); Clear solution

BIOLOGICAL ACTIVITY

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

IC50: 23 nM (HDAC9), 43 nM (HDAC7), 97 nM (HDAC5), 157 nM (HDAC4)[1]

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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.
- Patent. US20180263995A1.

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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.

Caution: Product has not been fully validated for medical applications. For research use only.

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