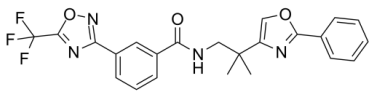
Data Sheet

Product Name:	TMP195
Cat. No.:	CS-7000
CAS No.:	1314891-22-9
Molecular Formula:	$C_{23}H_{19}F_3N_4O_3$
Molecular Weight:	456.42
Target:	HDAC
Pathway:	Cell Cycle/DNA Damage; Epigenetics
Solubility:	DMSO : ≥ 100 mg/mL (219.10 mM)



BIOLOGICAL ACTIVITY:

TMP195 is a selective class IIa histone deacetylase (**HDAC**) inhibitor with an **IC_{50}** of 300 nM. IC50 & Target: IC50: 300 nM (HDAC), 9 nM (HDAC9), 46 nM (HDAC7), 106 nM (HDAC5) , 111 nM (HDAC4), 11700 nM (HDAC8), 47800 nM (HDAC6)[1] **In Vitro:** TMP195 blocks the accumulation of CCL2 protein in the supernatants of monocyte-derived macrophage differentiation cultures. TMP195 significantly increases the amount of CCL1 protein secreted by the monocytes compared to vehicle group. In the transcriptional profiling data from the PHA-stimulated PBMC experiments, CCL2 and CCL1 are respectively down- or upregulated by TMP195[1]. TMP195 occupies the acetyllysine-binding site of class IIa HDACs. TMP195 competes against binding of HDAC7 to a variety of side-chain modifications on the same peptide backbone, despite no interference with the activity of other acetyllysine reader proteins BRD4 (IC_{50}>50 μM)[2]. **In Vivo:** TMP195 treatment alters the tumour microenvironment and reduces tumour burden and pulmonary metastases by modulating macrophage phenotypes. TMP195 induces the recruitment and differentiation of highly phagocytic and stimulatory macrophages within tumors. Combining TMP195 with chemotherapy regimens or T-cell checkpoint blockade in this model significantly enhances the durability of tumour reduction[2].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [2]Recombinant HDAC7 catalytic domain (amino acids 483-903) is labeled with DyLight 650 and applied to an arrayed library of 3,868 immobilized 20-mer peptides. Arrays are conducted using an automated TECAN HS4 microarray processing station, initiated by incubation with blocking buffer for 30 min at 30°C followed by ishing with saline containing 50 mM Tris Base and 0.1% Tween-20 (pH 7.2) before incubation with the labeled HDAC7 protein for 120 min at 4°C. In the case of TMP195 competition experiments, the labeled protein is pre-incubated with TMP195 for 30 min before application to the array. The microarrays are then ished before being dried and imaged with an scanner[2]. **Animal Administration:** [2]Mouse: For all mouse experiments, mice are treated with intraperitoneal (i.p.) injections of 50 μL of the vehicle dimethyl sulfoxide (DMSO) or 50 μL of TMP195 dissolved in 100% DMSO at a final concentration of 50 mg per kg daily[2].

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]. Guerriero JL, et al. Class IIa HDAC inhibition reduces breast tumors and metastases through anti-tumor macrophages. Nature. 2017 Mar 16;543(7645):428-432.

CAIndexNames:

Benzamide, N-[2-methyl-2-(2-phenyl-4-oxazolyl)propyl]-3-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-

SMILES:

O=C(NCC(C)(C)C1=COC(C2=CC=CC=C2)=N1)C3=CC(C4=NOC(C(F)(F)F)=N4)=CC=C3

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA