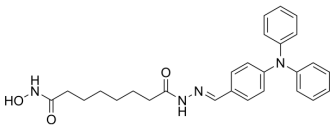
WT-161

Cat. No.:	HY-100871
CAS No.:	1206731-57-8
Molecular Formula:	$C_{27}H_{30}N_4O_3$
Molecular Weight:	458.55
Target:	HDAC; Apoptosis; Beta-lactamase
Pathway:	Cell Cycle/DNA Damage; Epigenetics; Apoptosis; Anti-infection
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (218.08 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1808 mL	10.9039 mL	21.8079 mL
5 mM	0.4362 mL	2.1808 mL	4.3616 mL
10 mM	0.2181 mL	1.0904 mL	2.1808 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 (5.45 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.45 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.45 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

WT-161 is a potent and selective HDAC6 inhibitor with an IC_{50} of 0.40 nM[1]. WT-161 also inhibits metallo-β-lactamase domain-containing protein 2 (MBLAC2)[2].

IC_{50} & Target

HDAC6 0.4 nM (IC_{50})	HDAC1 8.35 nM (IC_{50})	HDAC2 15.4 nM (IC_{50})	HDAC3 51.6 nM (IC_{50})
HDAC8			

	1430 nM (IC_{50})
In Vitro	WT161 selectively inhibits HDAC6 and dramatically increases levels of acetylated α-tubulin (Ac-α-tubulin) with little effect on global lysine acetylation. WT161 induces significant toxicity in all multiple myeloma cell lines tested, with IC_{50}s between 1.5 and 4.7 μM . WT161 in combination with bortezomib triggers significant accumulation of polyubiquitinated proteins and cell stress, followed by caspase activation and apoptosis. More importantly, this combination treatment is effective in bortezomib-resistant cells and in the presence of bone marrow stromal cells, which have been shown to mediate multiple myeloma cell drug resistance[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	WT161 shows toxicity at 100 mg/kg i.p., but WT161 is well tolerated at 50 mg/kg i.p.. Bortezomib combined with WT161 demonstrates a significant antitumor effect[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	MM.1S cells are treated with increasing concentrations of WT161 (0-10 μM) for 48 hours. Cell viability is determined using the MTT assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Mice tumor xenograft are assigned into cohorts receiving vehicle (control), BTZ (0.5 mg/kg, i.v.), WT161 (50 mg/kg, i.p.), or BTZ+WT161. WT161 is administered for five consecutive days each week, and BTZ is given on a twice-weekly schedule. Caliper measurements of the longest perpendicular tumor diameters are performed on alternate days to estimate the tumor volume[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Death Dis. 2023 Apr 6;14(4):250.
- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.
- Biosci Rep. 2021 Apr 30;41(4):BSR20203905.
- J Appl Toxicol. 2023 Mar 1.
- Research Square Preprint. 2021 Jun.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Severin Lechner, et al. Target deconvolution of HDAC pharmacopoeia reveals MBLAC2 as common off-target. Nat Chem Biol. 2022 Apr 28.

[2]. Hideshima T, et al. Discovery of selective small-molecule HDAC6 inhibitor for overcoming proteasome inhibitor resistance in multiple myeloma. Proc Natl Acad Sci U S A. 2016 Nov 15;113(46):13162-13167.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA