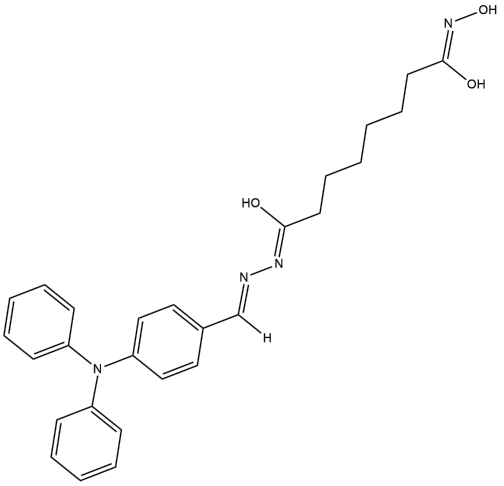
Product Data Sheet

Product Name: WT161
Cat. No.: GC18206

Chemical Properties

Cas. No.	1206731-57-8		
Chemical Name	8-(hydroxyamino)-8-oxo-octanoic acid, 2-[[4-(diphenylamino)phenyl]methylene]hydrazide		
SMILES	ONC(CCCCCCC(N/N=C/C(C=C1)=CC=C1N(C2=CC=CC=C2)C3=CC=CC=C3)=O)=O		
Formula	$C_{27}H_{30}N_4O_3$	M.Wt	458.6
Solubility	DMF: 10 mg/ml,DMSO: 10 mg/ml,DMSO:PBS (pH 7.2) (1:2): 0.33 mg/ml	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

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Cell experiment: 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].

Animal experiment: 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].

References:

[1]. 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.

Background

WT-161 is a potent and selective HDAC6 inhibitor with an IC50 of 0.40 nM.

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 IC50s 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].

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].

References:

[1]. 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.