

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(CCCCCC(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

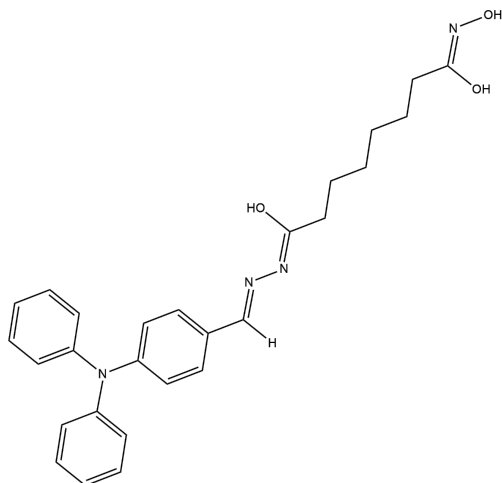
Solubility DMF: 10 mg/ml, DMSO: 10 mg/ml, DMSO: PBS (pH 7.2) (1:2): 0.33 mg/ml

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

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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Cell experiment: MM.1S cells are treated with increasing concentrations of WT161 (0-10 μ M) 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 μ M. 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

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