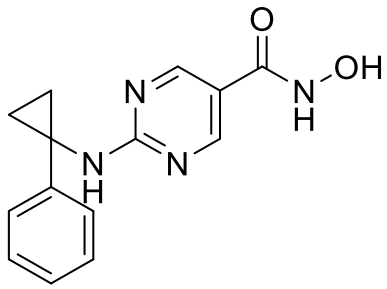
Product data sheet

MedKoo Cat#: 407295 Name: ACY-738 CAS#: 1375465-91-0 Chemical Formula: $C_{14}H_{14}N_4O_2$ Exact Mass: 270.1117 Molecular Weight: 270.292	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
ACY-738 is a potent and selective HDAC6 inhibitor with improved brain bioavailability. ACY-738 inhibits HDAC6 with low nanomolar potency and a selectivity of 60- to 1500-fold over class I HDACs. ACY-738 induces dramatic increases in α-tubulin acetylation in brain and stimulate mouse exploratory behaviors in novel, but not familiar environments.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	32	118.39

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.70 mL	18.50 mL	37.00 mL
5 mM	0.74 mL	3.70 mL	7.40 mL
10 mM	0.37 mL	1.85 mL	3.70 mL
50 mM	0.07 mL	0.37 mL	0.74 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Shi P, Hoang-Minh LB, Tian J, Cheng A, Basrai R, Kalaria N, Lebowitz JJ, Khoshbouei H, Deleyrolle LP, Sarkisian MR. HDAC6 Signaling at Primary Cilia Promotes Proliferation and Restricts Differentiation of Glioma Cells. Cancers (Basel). 2021 Apr 1;13(7):1644. doi: 10.3390/cancers13071644. PMID: 33915983; PMCID: PMC8036575.

2. Mithraprabhu S, Khong T, Jones SS, Spencer A. Histone deacetylase (HDAC) inhibitors as single agents induce multiple myeloma cell death principally through the inhibition of class I HDAC. Br J Haematol. 2013 Aug;162(4):559-62. doi: 10.1111/bjh.12388. Epub 2013 May 21. PMID: 23692150.

In vivo study

1. Regna NL, Vieson MD, Luo XM, Chafin CB, Puthiyaveetil AG, Hammond SE, Caudell DL, Jarpe MB, Reilly CM. Specific HDAC6 inhibition by ACY-738 reduces SLE pathogenesis in NZB/W mice. Clin Immunol. 2016 Jan;162:58-73. doi: 10.1016/j.clim.2015.11.007. Epub 2015 Nov 22. PMID: 26604012.

7. Bioactivity
Biological target:
ACY-738 inhibits HDAC6 with low nanomolar potency (IC50=1.7 nM) and a selectivity of 60- to 1500-fold over class I HDACs.

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In vitro activity

To confirm that the patient-derived L0 (high grade), S3 (high grade), and S7 (low grade) glioma cell lines are sensitive to HDAC6 inhibitors, dissociated cells in serum-free media were treated with different concentrations of ACY-738 (738). After five days, 0.5 to 5 µM treatment significantly reduced the size of L0 and S7 (Figure S1A–G) and S3 gliomaspheres (Figure S1K), suggesting decreased tumor cell proliferation. The proliferation of adherent murine KR158 glioma cells was also decreased following treatment with 5-µM 738 but remained unchanged with a lower concentration (500 nM) (Figure S1J). Compared to vehicle-treated cells, it was unexpectedly difficult to find aaTub+ cilia across S3, L0, and S7 human glioma cells following treatment with 738. The presence of aaTub+ cilia on S3 cells was reduced 1 h after treatment with 738 (Figure 1E). Importantly, the decrease in aaTub+ in cilia was not indicative of cilia loss because cilia were present and identified by co-labeling with an antibody against ADP ribosylation factor 13B (ARL13B) (Figure 1E). To assess whether HDAC6 inhibitors disrupted the microtubular structure of the ciliary axoneme, leading to the reduced aaTub observed by immunostaining, the cilia of treated cells were examined using TEM. The ciliary structure of L0 cells 24 h were fixed and examined after 5-µM 738 exposure; it was found that cilia with organized, longitudinally aligned arrays of microtubules along the axoneme (Figure S3A,B), suggesting that the ciliary microtubular structure was conserved following treatment with 738.

Reference: Cancers (Basel). 2021 Apr 1;13(7):1644. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/33915983/

In vivo activity

From 22 to 38weeks-of-age, mice were injected intraperitoneally with 5 or 20mg/kg of ACY-738, or vehicle control. Body weight and proteinuria were measured every 2weeks, while sera anti-dsDNA, Ig isotypes, and cytokine levels were measured every 4weeks. Kidney disease was determined by evaluation of sera, urine, immune complex deposition, and renal pathology. Flow cytometric analysis assessed thymic, splenic, bone marrow, and peripheral lymphocyte differentiation patterns. The results showed HDAC6 inhibition decreased SLE disease by inhibiting immune complex-mediated glomerulonephritis, sera anti-dsDNA levels, and inflammatory cytokine production and increasing splenic Treg cells. Inhibition of HDAC6 increased the percentage of cells in the early-stage developmental fractions of both pro- and pre-B cells. These results suggest that specific HDAC6 inhibition may be able to decrease SLE disease by altering aberrant T and B cell differentiation.

Reference: Clin Immunol. 2016 Jan;162:58-73. https://linkinghub.elsevier.com/retrieve/pii/S1521-6616(15)30064-4