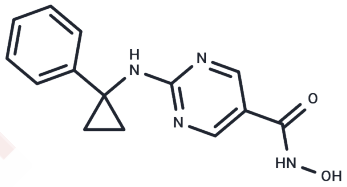
Data Sheet (Cat.No.T3509)

TargetMol

ACY-738

Chemical Properties



CAS No. : 1375465-91-0

Formula: C14H14N4O2

Molecular Weight: 270.29

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	ACY-738 demonstrates inhibitory activity against recombinant HDAC6 (IC50: 1.7 nM), with respective average selectivity over class I HDACs being 100-fold.
Targets(IC50)	HDAC
In vitro	ACY-738 increases the acetylated (lysine 40) fraction of α-tubulin in RN46A-B14 cells at the concentration of 2.5?μM. The effect that ACY-738 (10 μM) induces cell death is similar to LBH589 and FK228.
In vivo	ACY-738 administered at a dosage of 5 mg/kg notably increases α-tubulin acetylation in whole-brain lysates, whereas a higher dosage (50 mg/kg) fails to enhance locomotor activity in wild-type (WT) mice within a home cage setting. At a dosage of 5 mg/kg by body weight (BW), ACY-738 influences B cell differentiation in bone marrow (BM) without significantly impacting immunoglobulin G (IgG) and complement component 3 (C3) deposition in NZB/W mice. This dosage also achieves a peak plasma concentration of 1310 ng/mL approximately 0.0830 hours post-treatment. When the dosage is increased to 20 mg/kg, ACY-738 markedly reduces the severity of proteinuria in NZB/W F1 mice and significantly lowers anti-double-stranded DNA (anti-dsDNA) production as well as glomerular interleukin-6 (IL-6) and interleukin-10 (IL-10) mRNA levels by more than 50% in NZB/W mice; the latter being reduced to non-detectable levels with the 20 mg/kg treatment. Additionally, both 5 and 20 mg/kg dosages of ACY-738 decrease serum interleukin-1 beta (IL-1β) production as the NZB/W mice age.
Kinase Assay	Recombinant kinase domain of EGFR L858R and T790M-L858R mutants are incubated with EGF816 to confirm covalent modification of EGFR and site of adduction. Recombinant enzyme is incubated at room temperature with a 20-fold molar excess of compound in 40 mM Tris, pH 8, 500 mM NaCl, 1% glycerol, 5 mM TCEP for 1 h. The reaction is quenched by addition of dithiothreitol (DTT, 80-fold excess to compound) and transfer to ice. A third of the reaction (10 μL) is processed for intact MS by adding an equal volume of 6 M Guan HCl, 100 mM Tris, pH 8, 20 mM DTT, 10 mM TCEP and incubating at room temperature for 15 min. Intact MS analysis is performed on an Agilent 6520 QToF mass spectrometer equipped with a dual spray ion source (IS of 4500 V, fragmentor of 250 V, fas temp of 350°C, and skimmer of 75 V). The samples are injected onto a PLRP-S column (2.1 mm × 50 mm), heated to 60°C, and desalted for 2 min at 500 μL/min and 3% B prior to elution with a fast gradient of 3-50% B in 3 min (B, 0.1% formic acid). The data are analyzed in MassHunter for automatic peak selection,

Kinase Assay	integration, and spectral deconvolution with a mass range of 15?000-75?000 Da.

Solubility Information

Solubility	DMSO: 50 mg/mL (184.99 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (7.4 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.6997 mL	18.4986 mL	36.9973 mL
5 mM	0.7399 mL	3.6997 mL	7.3995 mL
10 mM	0.370 mL	1.8499 mL	3.6997 mL
50 mM	0.074 mL	0.370 mL	0.7399 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Jochems J, et al Antidepressant-like properties of novel HDAC6-selective inhibitors with improved brain bioavailability. Neuropsychopharmacology. 2014 Jan;39(2):389-400.
Liu X, Cen X, Wu R, et al.ARIH1 activates STING-mediated T-cell activation and sensitizes tumors to immune checkpoint blockade.Nature Communications.2023, 14(1): 4066.