ACY-738

Cat. No.: HY-19327

CAS No.: 1375465-91-0

Molecular Formula: $C_{14}H_{14}N_4O_2$

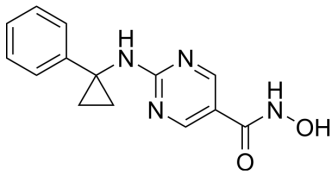
Molecular Weight: 270.29

Target: HDAC

Pathway: Cell Cycle/DNA Damage; Epigenetics

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 : ≥ 32 mg/mL (118.39 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.6997 mL	18.4986 mL	36.9973 mL
5 mM	0.7399 mL	3.6997 mL	7.3995 mL
10 mM	0.3700 mL	1.8499 mL	3.6997 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: ≥ 2.08 mg/mL (7.70 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (7.70 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (7.70 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ACY-738 is a potent, selective and orally-bioavailable HDAC6 inhibitor, with an IC_{50} of 1.7 nM; ACY-738 also inhibits HDAC1, HDAC2, and HDAC3, with IC_{50}s of 94, 128, and 218 nM.

IC_{50} & Target	HDAC6	HDAC1	HDAC2	HDAC3
	1.7 nM (IC_{50})	94 nM (IC_{50})	128 nM (IC_{50})	218 nM (IC_{50})

In Vitro	ACY-738 (2.5 μM) increases the acetylated (lysine 40) fraction of α-tubulin in RN46A-B14 cells[1]. ACY-738 (10 μM) induces cell death comparable to LBH589 and FK228[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ACY-738 (5 mg/kg) leads to significant increase in α-tubulin acetylation in whole-brain lysates. ACY-738 (50 mg/kg) fails to produce an enhancement of locomotor activity in WT mice tested in a home cage environment[1]. ACY-738 (5 mg/kg) reaches a maximum plasma concentration of 1310 ng/mL at 0.0830 h following treatment. ACY-738 (5 mg/kg BW) alters BM B cell differentiation, but shows no significant effect on IgG and C3 deposition in NZB/W mice. ACY-738 (20 mg/kg) significantly attenuates the severity of proteinuria in NZB/W F1 mice. ACY-738 (5 mg/kg) shows a significant decrease in anti-dsDNA production in NZB/W mice as they aged. ACY-738 (5, 20 mg/kg) attenuates sera IL-1β production as the NZB/W mice aged. ACY-738 (5 mg/kg) significantly reduces glomerular IL-6 and IL-10 mRNA levels by more than 50% while treatment with 20 mg/kg ACY-738 reduced IL-6 and IL-10 mRNA to non-detectable levels[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice are injected i.p. 5 days/week with the vehicle control (DMSO), ACY-738 treatment at 5 mg/kg (low-dose), or ACY-738 treatment at 20 mg/kg (high-dose) beginning at 22-weeks-of-age until euthanasia at 38 weeks-of-age. The total volume injected is 80 μL. Proteinuria and weight are measured every 2 weeks and blood is collected every four weeks for sera analysis. Proteinuria is measured by a standard semi-quantitative test using Siemens Uristix dipsticks. Results are quantified and scored as follows: dipstick reading of 0 mg/dL = 0, trace = 1, 30-100 mg/dL = 2, 100-300 mg/dL = 3, 300-2000 mg/dL = 4, and 2000 + mg/dL = 5[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Lett. 2022 Sep 16;215911.
- Cell Death Dis. 2023 Apr 6;14(4):250.

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REFERENCES

[1]. Jochems J, et al. Antidepressant-like properties of novel HDAC6-selective inhibitors with improved brain bioavailability. Neuropsychopharmacology. 2014 Jan;39(2):389-400.

[2]. Regna NL, et al. Specific HDAC6 inhibition by ACY-738 reduces SLE pathogenesis in NZB/W mice. Clin Immunol. 2016 Jan;162:58-73.

[3]. Mithraprabhu S, et al. 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.

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