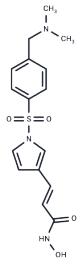
Data Sheet (Cat.No.T6637)

TargetMol

Resminostat

Chemical Properties



CAS No. : 864814-88-0

Formula: C16H19N3O4S

Molecular Weight: 349.4

Storage: Store at low temperature
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	Resminostat (4SC-201) is an orally bioavailable inhibitor of histone deacetylases (HDACs) with potential antineoplastic activity.
Targets(IC50)	HDAC
In vitro	Resminostat exhibits a favorable pharmacokinetic (PK) profile with high bioavailability and low intersubject variability in plasma concentration over time (low pT variability). The apparent half-life (t 1/2) of orally administered Resminostat ranges between 2.7 to 4.4 hours. A once-daily oral dose of 600 mg Resminostat is well-tolerated for 1-5 days within a 14-day cycle.
In vivo	Resminostat activates Caspases 3, 8, and 9, and synergizes with Melphalan and Proteasome inhibitors bortezomib and S-2209. Resminostat [HCl] highly acetylates histone H4 in MM cells. It inhibits cell growth and strongly induces apoptosis in MM cell lines (OPM-2, NCI-H929, U266) and primary MM cells consistently. At 1 μM, Resminostat inhibits cell proliferation and induces G0/G1 cell cycle arrest in MM cell lines (OPM-2, NCI-H929, U266), accompanied by decreased levels of cyclin D1, CDC25A, CDK4, and Rb and upregulation of the p21 gene. It interferes with the Akt signaling pathway by reducing the phosphorylation of 4E-BP1 and p70S6K. Additionally, Resminostat increases the expression levels of Bim and Bax proteins while decreasing the level of Bcl-xL.
Kinase Assay	Enzymatic HDAC activity assays: 40 μL enzyme buffer (15 mM Tris HCl pH 8.1, 0.25 mM EDTA, 250 mM NaCl, 10% v:v glycerol) containing HDAC1, 3, 6 or 8 activity, 29 μL enzyme buffer and 1 μL resminostat at different concentrations are added to a 96-well microtitre plate and the reaction started by the addition of 30μL substrate peptide Ac-NH-GGK(Ac)-AMC (HDAC1, 3 and 6 assays, final concentrations 6 μM for HDAC1, 10 μM for HDAC6 and 25 μM for HDAC3/DAD) or Ac-RHK(Ac)K(Ac)-AMC (HDAC8 assay, final concentration 50 μM). After incubation for 3 hours (HDAC1, HDAC6, HDAC8) or 2 hours (HDAC3) at 30°C, the reaction is terminated by the addition of 25 μL stop solution (50 mM Tris HCl pH 8, 100 mM NaCl, 0.5 mg/mL trypsin and 2 μM trichostatin A [TSA]). After incubation at room temperature for further 40 min, fluorescence is measured using a multilabel counter (extinction 355 nm, emission 460 nm) for quantification of AMC generated by tryptic cleavage of the deacetylated peptide. For the calculation of the IC50, the fluorescence in wells without test compound (1% DMSO, negative control) is set as 100% enzymatic

Kinase Assay	activity and the fluorescence in wells with 2 μM TSA (positive control) is set at 0% enzymatic activity (background fluorescence substracted).
Cell Research	Cell lines: OPM-2,NCI-H929,RPMI-8226 and U266. Concentrations: ~ 10 μM. Method: WST-1 assay

Solubility Information

Solubility	DMSO: 65 mg/mL (186.03 mM),Sonication is recommended. Ethanol: 65 mg/mL (186.03 mM),Sonication is recommended. H2O: <1 mg/mL, (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 5 mg/mL (14.31 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	2.862 mL	14.3102 mL	28.6205 mL
5 mM	0.5724 mL	2.862 mL	5.7241 mL
10 mM	0.2862 mL	1.431 mL	2.862 mL
50 mM	0.0572 mL	0.2862 mL	0.5724 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

Mandl-Weber S, et al. Br J Haematol, 2010, 149(4), 518-528.
J.E. Ang, et al. EJC Supplements, 2008, 6(12), 123-124.