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产品名称：Resminostat (hydrochloride)
产品别名：RAS2410 hydrochloride; 4SC-201 hydrochloride

生物活性：

Description	Resminostat hydrochloride is a potent inhibitor of HDAC1, HDAC3 and HDAC6, with mean IC50 values of 42.5, 50.1, 71.8 nM, respectively, and shows less potent activities against HDAC8, with an IC50 of 877 nM.

IC_{50} & Target	HDAC1	HDAC3	HDAC6	HDAC8
	42.5 nM (IC_{50})	50.1 nM (IC_{50})	71.8 nM (IC_{50})	877 nM (IC_{50})

In Vitro	Resminostat hydrochloride (Resminostat [HCl], 5 μM) induces histone acetylation in myeloma cells. Resminostat hydrochloride displays a substrate competitive binding mode with a mean Ki value of 27 nM. Resminostat hydrochloride (5 μM) induces histone hyperacetylation in myeloma cells. Resminostat inhibits cell growth, induces apoptosis and inhibits MM cell proliferation. Resminostat (5 μM) also modulates expression of bcl-2 family proteins and inhibits Akt pathway signalling downstream of Akt. Resminostat exerts synergistic activity against myeloma cells when combined with common and new anti-myeloma agents[1]. Resminostat inhibits cell growth in head and neck squamous cell carcinoma cell lines, with IC50s ranging from 0.775 μM to 1.572 μM (IC50 for SCC25: 0.775 μM; CAL27: 1.572 μM; and FaDu: 0.899 μM). Resminostat (1.25 and 2.5 μM) has a synergistic effect with irradiation on HNSCC cell lines. Resminostat in combination with cisplatin induces a downregulation of survivin. However, Resminostat shows no effect on Mcl-1 and p-AKT expression[2]. Resminostat reduces viability of HCC cells with the co-treatment of AZD-2014, with IC50s ranging from 0.89 ± 0.12 μM to 0.07 ± 0.01 μM[3].

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (129.58 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5915 mL	12.9577 mL	25.9155 mL
	5 mM	0.5183 mL	2.5915 mL	5.1831 mL
	10 mM	0.2592 mL	1.2958 mL	2.5915 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

Solubility: ≥ 2.5 mg/mL (6.48 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (6.48 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.48 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.48 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Mandl-Weber S, et al. The novel inhibitor of histone deacetylase resminostat (RAS2410) inhibits proliferation and induces apoptosis in multiple myeloma (MM) cells. Br J Haematol. 2010 May;149(4):518-28. [2]. Enzenhofer E, et al. Effect of the histone deacetylase inhibitor resminostat on head and neck squamous cell carcinoma cell lines. Head Neck. 2017 May;39(5):900-907. [3]. Peng X, et al. mTOR inhibition sensitizes human hepatocellular carcinoma cells to resminostat. Biochem Biophys Res Commun. 2016 Sep 2;477(4):556-562.

实验参考：

Cell Assay	A CCK-8 cell proliferation assay is used to investigate the antiproliferative effect of resminostat on HNSCC cells. Cells are seeded into 96-well plates at a density of 3 × 10^5/well. After 24 hours of growth, the cells are treated with resminostat and cisplatin, either alone or in combination and incubated for 72 hours. Untreated cells maintained in RPMI and equal concentrations of dimethylsulfoxide served as control. After 72 hours, cell proliferation is measured by CCK-8. Experiments are carried out in triplicate 3 times[2].
Kinase Assay	Forty microliter 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 [HCl] at different concentrations are added to a 96-well microtitre plate and the reaction started by the addition of 30 μL 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 180 min (HDAC1, HDAC6, HDAC8) or 120 min (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 Wallac Victor2 1420 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 50% inhibitory concentration (IC50) values the fluorescence in wells without test compound (1% DMSO, negative control) is set as 100% enzymatic activity and the fluorescence in wells with 2 μM TSA (positive control) are set at 0% enzymatic activity (background fluorescence substracted)[1].
	[1]. Mandl-Weber S, et al. The novel inhibitor of histone deacetylase resminostat (RAS2410) inhibits proliferation and induces apoptosis in multiple myeloma (MM) cells. Br J Haematol. 2010 May;149(4):518-28.

References	[2]. Enzenhofer E, et al. Effect of the histone deacetylase inhibitor resminostat on head and neck squamous cell carcinoma cell lines. Head Neck. 2017 May;39(5):900-907. [3]. Peng X, et al. mTOR inhibition sensitizes human hepatocellular carcinoma cells to resminostat. Biochem Biophys Res Commun. 2016 Sep 2;477(4):556-562.