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产品名称：ACY-775
产品别名：ACY-775

生物活性：

Description	ACY-775 is a potent and selective inhibitor of the of histone deacetylase 6 (HDAC6) with an IC_{50} of 7.5 nM.			
IC_{50} & Target	HDAC6	HDAC1	HDAC2	HDAC3
	7.5 nM (IC_{50})	2123 nM (IC_{50})	2570 nM (IC_{50})	11223 nM (IC_{50})
In Vitro	In vehicle-treated cells, α-tubulin is mainly presented in the deacetylated form, while histone 3 is clearly acetylated. Upon treatment with ACY-775, a clear enhancement of the acetylation of α-tubulin is visible, while histone acetylation remains unaltered. Acetylation of α-tubulin is visualized by immunofluorescence and the intensity in the neurites of the neurons is quantified and normalized to the length of the fluorescent signal. In vehicle-treated DRG neurons, acetylated α-tubulin is already present. Upon treatment with ACY-775 the signal intensity of acetylated α-tubulin increases significantly. Significant increase in motility of mitochondria and also the total number of mitochondria within the neurites are observed compare with vehicle-treated DRG neurons. A significantly higher number of retrogradely transport mitochondria is observed in DRG neurons treated with ACY-775 compare with vehicle-treated cells[1].			
In Vivo	Biodistribution profiles of ACY-738, ACY-775, and tubastatin A are examined after acute dosing at 5 or 50 mg/kg over 2 h. At t=30 min after acute 50 mg/kg injection, respective plasma levels of ACY-738 and ACY-775 are 515 ng/mL (1.9 μM) and 1359 ng/mL (4.1 μM). Elimination from plasma is rapid, with plasmatic half-life of 12 min and concentration below 10 ng/mL after 2 h. Nevertheless, areas under concentration time curves for brain and plasm calculated over 2 h for both ACY-738 and ACY-775 lead to ratios >1. When ACY-738 (5 mg/kg) or ACY-775 (50 mg/kg) are administered repeatedly in wild-type mice at 24 h, 4 h, and 30 min before killing, significant increases in α-tubulin acetylation are observed in all tested brain regions[2].			
Solvent&Solubility	***In Vitro:*** **DMSO : 25 mg/mL (75.68 mM;** Need ultrasonic)			

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	3.0270 mL	15.1350 mL	30.2700 mL
	5 mM	0.6054 mL	3.0270 mL	6.0540 mL
	10 mM	0.3027 mL	1.5135 mL	3.0270 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→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (7.57 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.57 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 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (7.57 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.57 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (7.57 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.57 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]. Veronick Benoy, et al. Development of Improved HDAC6 Inhibitors as Pharmacological Therapy for Axonal Charcot-Marie-Tooth Disease. Neurotherapeutics. 2017 Apr; 14(2): 417-428. [2]. Jeanine Jochems et al. Antidepressant-Like Properties of Novel HDAC6-Selective Inhibitors with Improved Brain Bioavailability. Neuropsychopharmacology. 2014 Jan; 39(2): 389-400.

实验参考：

Cell Assay	Undifferentiated RN46A-B14 cells, a line of immortalized rat raphe neuronal precursors, are grown. They are treated with 2.5 μM ACY-738, ACY-775, tubastatin A, 0.6 μM TSA or vehicle (0.1% DMSO) for 4 h. Samples are processed using histone extraction kit and quantified using protein assay. [2]
Animal Administration	Mice are tested for immobility in the TST. At 30 min or 2 h after i.p. injection of ACY-738 (5, 50 mg/kg), ACY-775 (5, 50 mg/kg), and citalopram (0.5, 2, 20 mg/kg), a combination of the previous, or vehicle, mice are attached to the test rig and time immobile over 6 min is recorded. For open-field activity mice are injected with ACY-738 or ACY-775 at 5, 10, or 50 mg/kg or vehicle and allowed to explore. Activity is recorded[2].
References	[1]. Veronick Benoy, et al. Development of Improved HDAC6 Inhibitors as Pharmacological Therapy for Axonal Charcot-Marie-Tooth Disease. Neurotherapeutics. 2017 Apr; 14(2): 417-428. [2]. Jeanine Jochems et al. Antidepressant-Like Properties of Novel HDAC6-Selective Inhibitors with Improved Brain Bioavailability. Neuropsychopharmacology. 2014 Jan; 39(2): 389-400.