上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：ACY-738
产品别名：ACY-738

生物活性：

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].			
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].			

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

*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 (9.25 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (9.25 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 (9.25 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (9.25 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 (9.25 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (9.25 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]. 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.

实验参考：

Animal Administration	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].
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.