产品名称：**PCI-34051**
产品别名：**PCI-34051**

生物活性：

Description

PCI-34051 is a potent and selective HDAC8 inhibitor with IC_{50} of 10 nM, with >200-fold selectivity over the other HDAC isoforms.

IC_{50} & Target

HDAC8	HDAC6	HDAC1	HDAC10
10 nM (IC_{50})	2.9 μM (IC_{50})	4 μM (IC_{50})	13 μM (IC_{50})

In Vitro

PCI-34051 inhibits pure recombinant HDAC8 with Ki of 10 nM with >200-fold selectivity over the other HDACs tested, including HDACs 1, 2, 3, 6 and 10. PCI-34051 is derived from a low molecular weight hydroxamic acid scaffold that possessed promising potency (HDAC8; Ki=2 μM) and selectivity (approximately fivefold) for HDAC8 relative to the other class I HDACs. PCI-34051 is found to induce apoptosis at low micromolar concentrations in cell lines derived from T-cell lymphomas, including Jurkat and HuT78, whereas doses as high as 20 μM has no effect on B-cell- or myeloid-derived lymphomas or solid tumor lines[1].

In Vivo

Administration of PCI-34051 and Dexamethasone reduces the eosinophilic inflammation and airway hyperresponsiveness in asthma to reduce the airway remodeling[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 30 mg/mL (101.24 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.3747 mL	16.8736 mL	33.7473 mL
5 mM	0.6749 mL	3.3747 mL	6.7495 mL
10 mM	0.3375 mL	1.6874 mL	3.3747 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 (8.44 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (8.44 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 (8.44 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (8.44 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 (8.44 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.44 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]. Balasubramanian S, et al. A novel histone deacetylase 8 (HDAC8)-specific inhibitor PCI-34051 induces apoptosis in T-cell lymphomas. Leukemia. 2008 May;22(5):1026-34. [2]. Ren Y, et al. Therapeutic effects of histone deacetylase inhibitors in a murine asthma model. Inflamm Res. 2016 Dec;65(12):995-1008.

实验参考：

Cell Assay	Tumor cell lines and human umbilical vein endothelial cells are cultured for at least two doubling times, and growth is monitored at the end of compound exposure using an Alamar Blue fluorometric cell proliferation assay as recommended by the manufacturer. Compounds (e.g.,PCI-34051) are assayed in triplicate wells in 96-well plates. The concentration required to inhibit cell growth by 50% (GI_{50}) and 95% confidence intervals are estimated from nonlinear regression using a four-parameter logistic equation[1]
Animal Administration	Mice[2] A mouse model of asthma is utilized. Briefly, healthy female BALB/C mice (n=72) aged 6-8 weeks and weighing 18-22 g are used. Animals are housed independently in a pathogen-free room and provided ad libitum access to water and standard food. Animals are housed for 1 week prior to experiment onset. Mice are divided into six treatment groups: normal control, simple asthma, Dexamethasone, Tubastatin A HCl, PCI-34051, and Givinostat. Sensitization is carried out for mice in the last five groups on the 1st, 8th and 15th day using ovalbumin (OVA, 20 μg) and aluminum hydroxide gel (2 mg). 7 days after the last sensitization, OVA (20 mg/mL) atomization is performed using an ultrasonic atomizing device (3 mL/min for 30 min, 3 times/week for 8 weeks). Dexamethasone (2.0 mg/kg), TSA (0.5 mg/kg), PCI-34051 (0.5 mg/kg) and Givinostat (0.5 mg/kg) are administered via intraperitoneal injection 30 min before excitation. In the normal control group, normal saline is used instead of OVA.
Kinase Assay	Histone deacetylase activity is measured using a continuous trypsin-coupled assay. For inhibitor characterization, measurements are performed in a reaction volume of 100 μL^{-1} using 96-well assay plates in a fluorescence plate reader. For each isozyme, the HDAC protein in reaction buffer (50 mM HEPES, 100 mM KCl, 0.001% Tween-20, 5% DMSO, pH 7.4, supplemented with bovine serum albumin at concentrations of 0-0.05%) is mixed with inhibitor at various concentrations and allowed to incubate for 15 min. Trypsin is added to a final concentration of 50 nM, and acetyl-Gly-Ala-(N-acetyl-Lys)-amino-4-methylcoumarin is added to a final concentration of 25-100 μM to initiate the reaction. After a 30 min lag time, the fluorescence is measured over a 30 min time frame using an excitation wavelength of 355 nm and a detection wavelength of 460 nm. The increase in fluorescence with time is used as the measure of the reaction rate. Inhibition constants Ki(app) are obtained using the program BatchKi[1].

References	[1]. Balasubramanian S, et al. A novel histone deacetylase 8 (HDAC8)-specific inhibitor PCI-34051 induces apoptosis in T-cell lymphomas. Leukemia. 2008 May;22(5):1026-34. [2]. Ren Y, et al. Therapeutic effects of histone deacetylase inhibitors in a murine asthma model. Inflamm Res. 2016 Dec;65(12):995-1008.

源叶生物