产品名称：CAY10603
产品别名：BML-281

生物活性：

Description

CAY10603 (BML-281) is a potent and selective HDAC6 inhibitor, with an IC_{50} of 2 pM; CAY10603 (BML-281) also inhibits HDAC1, HDAC2, HDAC3, HDAC8, HDAC10, with IC_{50}s of 271, 252, 0.42, 6851, 90.7 nM.

IC_{50} & Target

HDAC6	HDAC3	HDAC10	HDAC2	HDAC1	HDAC8
0.002 nM (IC_{50})	0.42 nM (IC_{50})	90.7 nM (IC_{50}	252 nM (IC_{50})	271 nM (IC_{50})	6851 nM (IC_{50})

In Vitro

CAY10603 (Compound 7) shows potent inhibitory activities against pancreatic cancer cell lines, with IC_{50}s of 1, 0.3, 0.1, 0.1, 0.6, <1, 0.5 μM for BxPC-3, HupT3, Mia Paca-2, Panc 04.03, SU.86.86, HMEC, HPDE6c7, respectively. CAY10603 (100 nM, 200-300 nM) is active against both the Mia Paca-2 and Panc04.03 cell lines[1]. CAY10603 inhibits HDAC6 deacetylase activity, and supresses the proliferation of lung adenocarcinoma cells. CAY10603 also induces apoptosis of lung adenocarcinoma cells. Furthermore, CAY10603 synergizes with gefitinib to induce apoptosis in lung adenocarcinoma cell lines, partly through the destabilization of EGFR and inactivation of the EGFR pathway[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (111.98 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2396 mL	11.1982 mL	22.3964 mL
5 mM	0.4479 mL	2.2396 mL	4.4793 mL
10 mM	0.2240 mL	1.1198 mL	2.2396 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 (5.60 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.60 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 (5.60 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.60 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 (5.60 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.60 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]. Kozikowski AP, et al. Use of the nitrile oxide cycloaddition (NOC) reaction for molecular probe generation: a new class of enzyme selective histone deacetylase inhibitors (HDACIs) showing picomolar activity at HDAC6. J Med Chem. 2008 Aug 14;51(15):4370-3. [2]. Wang Z, et al. HDAC6 promotes cell proliferation and confers resistance to gefitinib in lung adenocarcinoma. Oncol Rep. 2016 Jul;36(1):589-97.

实验参考：

Cell Assay	The pancreatic cancer cell lines BxPc-3, HupT3, Mia Paca-2, Panc 04.03, and SU 86.86 are obtained from ATCC and are grown in medium (DMEM or RPMI) containing 10% fetal calf serum and l-glutamine. Pancreatic cancer cells are plated out in duplicate into 6 wells of a 96-well microtiter plate at 2.5-4P103 cells per well. Four hours post plating, individual wells are treated with diluent (DMSO) or varying concentrations of SAHA or the indicated HDACIs from a concentration of 1 nm to 50 mm. Cytotoxicity is measured at time “0”, and 72 h post treatment using the colorimetric MTT assay. The IC_{50} values are calculated using XLfit. [1]
Kinase Assay	Purified HDACs are incubated with 1 mm carboxyfluorescein (FAM)-labeled acetylated peptide substrate and test compound for 17 h at 25°C in HDAC assay buffer containing 100 mm HEPES (pH 7.5), 25 mm KCl, 0.1% BSA, and 0.01% Triton X-100. Reactions are terminated by the addition of buffer containing 0.078% SDS for a final SDS concentration of 0.05%. Substrate and product are separated electrophoretically using a Caliper LabChip 3000 system with blue laser excitation and green fluorescence detection (CCD2). The fluorescence intensity in the substrate and product peaks is determined using the Well Analyzer software on the Caliper system. The reactions are performed in duplicate for each sample. IC_{50} values are automatically calculated using the IDBS XLFit version 4.2.1 plug-in for Microsoft Excel and the XLFit 4-Parameter Logistic Model (sigmoidal dose-response model): ((A+ ((B_A)/1+((C/x)D)))), in which x is compound concentration, A and B are respectively the estimated minimum and maximum of percent inhibition, C is the inflection point, and D is the Hill slope of the sigmoidal curve. [1]
References	[1]. Kozikowski AP, et al. Use of the nitrile oxide cycloaddition (NOC) reaction for molecular probe generation: a new class of enzyme selective histone deacetylase inhibitors (HDACIs) showing picomolar activity at HDAC6. J Med Chem. 2008 Aug 14;51(15):4370-3. [2]. Wang Z, et al. HDAC6 promotes cell proliferation and confers resistance to gefitinib in lung adenocarcinoma. Oncol Rep. 2016 Jul;36(1):589-97.