产品名称：**CUDC-101**
产品别名：**CUDC-101**

生物活性：

Description	CUDC-101 is a potent inhibitor of HDAC, EGFR, and HER2 with IC_{50}s of 4.4, 2.4, and 15.7 nM, respectively.

IC_{50} & Target

EGFR	HER2	HDAC	HDAC1	HDAC2	HDAC3
2.4 nM (IC_{50})	15.7 nM (IC_{50})	4.4 nM (IC_{50})	4.5 nM (IC_{50})	12.6 nM (IC_{50})	9.1 nM (IC_{50})
HDAC4	HDAC6	HDAC5	HDAC9	HDAC10	HDAC8
13.2 nM (IC_{50})	5.1 nM (IC_{50})	11.4 nM (IC_{50})	67.2 nM (IC_{50})	26.1 nM (IC_{50})	79.8 nM (IC_{50})
HDAC7					
373 nM (IC_{50})					

In Vitro

CUDC-101 inhibits both class I and class II HDACs, but not class III, Sir-type HDACs. CUDC-101 displays broad antiproliferative activity in many human cancer cell types. CUDC-101 is a potent and selective HDAC, EGFR, and HER2 inhibitor with only weak inhibition of the following protein kinases (IC50): KDR (VEGFR2) (849 nM), Src (11000 nM), Lyn (840 nM), Lck (5910 nM), Abl-1 (2890 nM), FGFR-2 (3430 nM), Flt-3 (1500 nM), and Ret (3200 nM)[1]. CUDC-101 (300 nM) inhibits both the full length AR (flAR) and the AR variant AR-V7[2]. CUDC-101 is the most active agent in all three ATC cell lines screened for inhibitors of EGFR and HDACs, with half-maximal inhibitory concentration (IC50) at 0.15 μM for 8505c, and 1.66 μM for both C-643 and SW-1736 cells. CUDC-101 inhibits cancer cell migration and modulates epithelial-mesenchymal transition marker expression in ATC cells. CUDC-101 also inhibits HDAC and MAPK pathway, induces p21, and decreases survivin and XIAP expression in ATC cells[3]. CUDC-101 (1 μM) increases the acetylation of p53 and α-tubulin, nonhistone substrates of HDAC, in treated cancer cells. CUDC-101 modulates RTK activity and expression and exhibits immediate and stable inhibition of RTK and downstream Akt signaling[4].

In Vivo

CUDC-101 (120 mg/kg, iv, daily) induces tumor regression in the Hep-G2 liver cancer model and is more efficacious than erlotinib at its maximum tolerated dose (MTD). In the erlotinib-resistant A549 NSCLC xenograft model, CUDC-101 (120 mg/kg) shows potent inhibition of tumor growth. In the erlotinib-sensitive H358 NSCLC models, CUDC-101 (15, 30, 60 mg/kg, i.v.) inhibits tumor growth in a dose-dependent manner. CUDC-101 (120 mg/kg) causes significant tumor regression in the lapatinib-resistant, HER2-negative, EGFR-overexpressing MDA-MB-468 breast cancer model and the EGFR-overexpressing CAL-27 head and neck squamous cell carcinoma (HNSCC) model. CUDC-101 (120 mg/kg) also inhibits tumor growth in the K-ras mutant HCT116 colorectal and EGFR/HER2 (neu)-expressing HPAC pancreatic cancer models[1]. In an in vivo mouse model of metastatic ATC, CUDC-101 inhibits tumor growth and metastases, and significantly prolongs survival[3]. CUDC-101 (120 mg/kg) is effective against a broad range of tumor types in xenograft models[4].

In Vitro:

DMSO : 25 mg/mL (**57.54 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing	1 mM	2.3015 mL	11.5077 mL	23.0155 mL

Solvent&Solubility	**Stock Solutions**	5 mM	0.4603 mL	2.3015 mL	4.6031 mL
		10 mM	0.2302 mL	1.1508 mL	2.3015 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 (5.75 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.75 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 (5.75 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (5.75 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

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。

References

[1]. Xiong Cai et al Discovery of 7-(4-(3-Ethynylphenylamino)-7-methoxyquinazolin-6-yloxy)-N-hydroxyheptanamide (CUDC-101) as a Potent Multi-Acting HDAC, EGFR, and HER2 Inhibitor for the Treatment of Cancer J. Med. Chem., 2010, 53 (5), pp 2000–2009

[2]. Lai CJ, et al. CUDC-101, a multitargeted inhibitor of histone deacetylase, epidermal growth factor receptor, and human epidermal growth factor receptor 2, exerts potent anticancer activity.Cancer Res. 2010 May 1;70(9):3647-56. Epub 2010 Apr 13.

[3]. Sun H, et al. CUDC-101, a Novel Inhibitor of Full-Length Androgen Receptor (flAR) and Androgen Receptor Variant 7 (AR-V7) Activity: Mechanism of Action and In Vivo Efficacy. Horm Cancer. 2016 Jun;7(3):196-210.

[4]. Zhang L, et al. Dual inhibition of HDAC and EGFR signaling with CUDC-101 induces potent suppression of tumor growth and metastasis in anaplastic thyroid cancer. Oncotarget. 2015 Apr 20;6(11):9073-85.

实验参考：

Cell Assay	Cancer cell lines are plated at 5000 to 10 000 cells per well in 96-well flat-bottomed plates with varying concentrations of compounds. The cells are incubated with compounds for 72 h in the presence of 0.5% of fetal bovine serum. Growth inhibition is assessed by an adenosine triphosphate (ATP) content assay using the Perkin-Elmer ATPlite kit. [1]
	Four- to six-week-old female athymic mice (nude nu/nu CD-1) are inoculated subcutaneously into the right hind flank region with 1 to 5×10^6 cells in a medium suspension of 100−200 μL. For

Animal Administration	orthotopic implantation of breast cancer cells, a cell suspension in 100 μL of medium is injected directly into the mammary fat pads through a 27G needle. Different doses of CUDC-101, standard anticancer agents and vehicle are administered orally, intraperitoneally, or via tail vein injection as indicated. [1]
Kinase Assay	The activities of Class I and II HDACs are assessed using the Biomol Color de Lys system. Briefly, HeLa cell nuclear extracts are used as a source of HDACs. Different concentrations of drugs are added to HeLa cell nuclear extracts in the presence of a colorimetric artificial substrate. Developer is added at the end of the assay and enzyme activity is measured in the Wallac Victor II 1420 microplate reader at 405 nM. [1]
References	[1]. Xiong Cai et al Discovery of 7-(4-(3-Ethynylphenylamino)-7-methoxyquinazolin-6-yloxy)-N-hydroxyheptanamide (CUDC-101) as a Potent Multi-Acting HDAC, EGFR, and HER2 Inhibitor for the Treatment of Cancer J. Med. Chem., 2010, 53 (5), pp 2000–2009 [2]. Lai CJ, et al. CUDC-101, a multitargeted inhibitor of histone deacetylase, epidermal growth factor receptor, and human epidermal growth factor receptor 2, exerts potent anticancer activity.Cancer Res. 2010 May 1;70(9):3647-56. Epub 2010 Apr 13. [3]. Sun H, et al. CUDC-101, a Novel Inhibitor of Full-Length Androgen Receptor (flAR) and Androgen Receptor Variant 7 (AR-V7) Activity: Mechanism of Action and In Vivo Efficacy. Horm Cancer. 2016 Jun;7(3):196-210. [4]. Zhang L, et al. Dual inhibition of HDAC and EGFR signaling with CUDC-101 induces potent suppression of tumor growth and metastasis in anaplastic thyroid cancer. Oncotarget. 2015 Apr 20;6(11):9073-85.