CUDC-101

Cat. No.: HY-10223

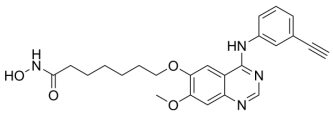
CAS No.: 1012054-59-9

Molecular Formula: $C_{24}H_{26}N_4O_4$

Molecular Weight: 434.49

Target: EGFR; HDAC

Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Cell Cycle/DNA Damage; Epigenetics



Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months

SOLVENT & SOLUBILITY

In Vitro

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

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3015 mL	11.5077 mL	23.0155 mL
	5 mM	0.4603 mL	2.3015 mL	4.6031 mL
	10 mM	0.2302 mL	1.1508 mL	2.3015 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 16.67 mg/mL (38.37 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.79 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.79 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.79 mM); Clear solution

BIOLOGICAL ACTIVITY

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. CUDC-101 is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target	EGFR 2.4 nM (IC_{50})	HER2 15.7 nM (IC_{50})	HDAC 4.4 nM (IC_{50})	HDAC1 4.5 nM (IC_{50})
	HDAC2 12.6 nM (IC_{50})	HDAC3 9.1 nM (IC_{50})	HDAC4 13.2 nM (IC_{50})	HDAC6 5.1 nM (IC_{50})
	HDAC5 11.4 nM (IC_{50})	HDAC9 67.2 nM (IC_{50})	HDAC10 26.1 nM (IC_{50})	HDAC8 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 (IC_{50}): 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 (IC_{50}) 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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

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.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay [1]

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.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal

Four- to six-week-old female athymic mice (nude nu/nu CD-1) are inoculated subcutaneously into the right hind flank region

Administration [1]	with 1 to 5×10^6 cells in a medium suspension of 100–200 μL. For 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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Elife. 2020 Dec 7;9:e61405.
- Am J Cancer Res. 2018 Dec 1;8(12):2402-2418
- Cancers (Basel). 2022 Mar 19;14(6):1575.
- Cancers. 2020 Jun 6;12(6):1484.

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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]. 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.

[3]. 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.

[4]. 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.

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