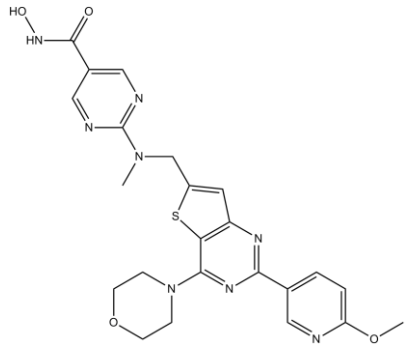
Product Name: CUDC-907

Revision Date: 6/30/2018

Product Data Sheet

Chemical Properties



Product Name:	CUDC-907
Cas No.:	1339928-25-4
M.Wt:	508.55
Formula:	C23H24N8O4S
Chemical Name:	N-hydroxy-2-[[2-(6-methoxypyridin-3-yl)-4-morpholin-4-ylthieno[3,2-d]pyrimidin-6-yl]methyl-methylamino]pyrimidine-5-carboxamide
Canonical SMILES:	CN(CC1=CC2=C(S1)C(=NC(=N2)C3=CN=C(C=C3)OC)N4CCOCC4)C5=NC=C(C=N5)C(=O)NO
Solubility:	≥25.45 mg/mL in DMSO, <2.5 mg/mL in EtOH, <2.34 mg/mL in H2O
Storage:	Store at -20°C
General tips:	For obtaining a higher solubility , please warm the tube at 37° C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20° C for several months.
Shopping Condition:	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request

Biological Activity

Targets :	DNA Damage/DNA Repair
Pathways:	HDAC

Description:

CUDC-907 is a dual-acting inhibitor of HDAC and PI3K with IC50 values of 1.7/5.0/1.8/2.8 nM (HDAC1/2/3/10) and 19/54/39 nM (PI3K).[1]
The phosphoinositide 3-kinases (PI3Ks) contain three classes of PI3K each with its own distinct lipid products and specific substrate. They are a family of lipid kinases that regulates a wide range of pathway by propagating intracellular signaling cascades. PI3K phosphorylates the 3'-OH group of phosphatidylinositols. This activated AKT, the protein Ser/Thr-kinase, by recruiting them to the

cell membrane. The PI3K/AKT signaling pathway is critical in cancer, because it promotes cell growth and survival. The studies have proved that PI3K pathway plays an important role in cancer progression and treatment for lung cancers, breast cancer.[2, 3] Histone deacetylases (HDACs) and histone acetyltransferases (HATs) mediates the balance between histone deacetylation and acetylation. HDACs also regulate the acetylation status of signaling molecules, chaperones, and transcription factors that are non-histone proteins.[4]
CUDC-907 is a potent inhibitor of class I PI3K kinases and HDAC classes I and II enzymes. CUDC-907 resulted in increase of acetylated histones and non-histone proteins such as tubulin and p53. CUDC-907 also induced p21 protein in H460 cell lines. CUDC-907 dose-dependently decreases phosphorylation of AKT and its downstream targets, p70S6 and 4EBP-1 by inhibiting the PI3K pathway,, in H460 cells. CUDC-907 were able to inhibit the activation of MEK in cancer cell lines including NSCLC H460 cells, breast cancer BT-474 cells and NSCLC H1975 cells. CUDC-907 suppresses the RAF- MEK-MAPK signaling pathway through HDAC inhibition. CUDC-907 can also cause the decrease of both p-SRC) and p-SRC in RPMI-8226 multiple myeloma cells. CUDC-907 induced cell-cycle arrest at G2–M phase at the dose of 1 μM for 24h.[1] CUDC-907 inhibited growth of the tumor in Daudi cancer cell xenografts dose-dependently. In a xenograft tumor model of DLBCL (SU-DHL4 diffuselarge B-cell lymphoma) CUDC-907 induced tumor regression after oral administration (100 mg/kg) or intravenous (50 mg/kg). CUDC-907 also caused tumor stasis in NSCLC cell xenografts [1].

***Reference**:*

[1]. Qian C, Lai CJ, Bao R, Wang DG, Wang J, Xu GX, Atoyan R, Qu H, Yin L, Samson M et al: Cancer network disruption by a single molecule inhibitor targeting both histone deacetylase activity and phosphatidylinositol 3-kinase signaling. Clin Cancer Res 2012, 18(15):4104-4113.
[2]. Wong KK, Engelman JA, Cantley LC: Targeting the PI3K signaling pathway in cancer. Curr Opin Genet Dev 2010, 20(1):87-90.
[3]. Engelman JA: Targeting PI3K signalling in cancer: opportunities, challenges and limitations. Nat Rev Cancer 2009, 9(8):550-562.
[4]. Kim HJ, Bae SC: Histone deacetylase inhibitors: molecular mechanisms of action and clinical trials as anti-cancer drugs. Am J Transl Res 2011, 3(2):166-179.

Protocol

Cell experiment:

Cell lines	H460 cells
Preparation method	The solubility of this compound in DMSO is > 25.5 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below - 20 °C for several months.
Reacting conditions	
Applications	In H460 cells, CUDC-907 increased the levels of activated caspase-7, p21 and c-PARP. Meanwhile, CUDC-907 decreased the levels of BCL-2, BCL-xL and survivin.

Animal experiment [3]:

Animal models	Daudi NHL xenograft mouse model
Dosage form	25, 50 or 100 mg/kg; p.o.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

***Reference**:*

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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