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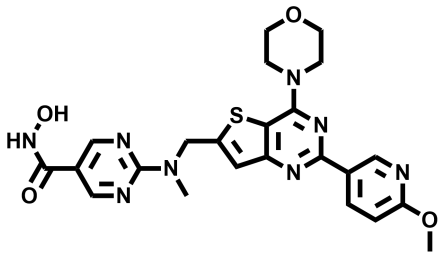
PI3K/HDAC dual inhibitor– CUDC-907

Chemical Name: N-hydroxy-2-(((2-(6-methoxypyridin-3-yl)-4-morpholinothieno[3,2-d]pyrimidin-6-yl)methyl)(methyl)amino)pyrimidine-5-carboxamide



Molecular Weight:	508.55
Formula:	$C_{23}H_{24}N_8O_4S$
Purity:	≥ 98%
CAS#:	1339928-25-4
Solubility:	DMSO up to 100 mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

Biological Activity:

CUDC-907 is a potent inhibitor of class I PI3K kinases with an IC_{50} of 19 nM, 54 nM, 311 nM and 39 nM for PI3Kα, PI3Kβ, PI3Kγ and PI3Kδ. It also potently inhibits HDAC1, HDAC2, HDAC3, HDAC6, HDAC10 and HDAC11 with IC_{50} of 1.7 nM, 5 nM, 1.8 nM, 27 nM, 2.8 nM and 5.4 nM respectively. Through its simultaneous HDAC inhibitory activity, CUDC-907 durably inhibits the PI3K-AKT-mTOR pathway and compensatory signaling molecules such as RAF, MEK, MAPK, and STAT-3, as well as upstream receptor tyrosine kinases. CUDC-907 induces apoptosis and G2–M cell-cycle arrest in cancer cells and effectively inhibits more than 50 different cancer cells' growth. It may potentially evade drug resistance in cancer cells. CUDC-907 also inhibits targets and tumor growth in xenograft tumor models. Currently CUDC-907 is in phase I clinical trials for patients with solid tumors or lymphoma.

How to Use:

In vitro: CUDC-907 was used at 0.1-1 μM final concentration in vitro and in cellular assays.

In vivo: CUDC-907 was orally dosed to mice at 100 mg/kg or intravenously dosed at 50 mg/kg once per day in the xenograft tumor model of SU-DHL4 (DLBCL) and A549 (NSCLC).

Reference:

1. Qian C, et al. Cancer network disruption by a single molecule inhibitor targeting both histone deacetylase activity and phosphatidylinositol 3-kinase signaling. (2012) Clin Cancer Res. 18(15):4104-13.
2. http://www.curis.com/CUDC_907_AACR_2012.pdf