产品名称：CUDC-907
产品别名：Fimepinostat

生物活性：

Description	Fimepinostat (CUDC-907) potently inhibits class I **PI3K**s as well as classes I and II **HDAC** enzymes with an **IC_{50}** of 19/54/39 nM and 1.7/5.0/1.8/2.8 nM for PI3Kα/PI3Kβ/PI3Kδ and HDAC1/HDAC2/HDAC3/HDAC10 , respectively.

IC_{50} & Target

PI3Kα	PI3Kβ	PI3Kδ	PI3Kγ	HDAC1
19 nM (IC_{50})	54 nM (IC_{50})	39 nM (IC_{50})	311 nM (IC_{50})	1.7 nM (IC_{50})
HDAC2	HDAC3	HDAC4	HDAC5	HDAC6
5 nM (IC_{50})	1.8 nM (IC_{50})	409 nM (IC_{50}	674 nM (IC_{50})	27 nM (IC_{50})
HDAC7	HDAC8	HDAC9	HDAC10	HDAC11
426 nM (IC_{50})	191 nM (IC_{50})	554 nM (IC_{50})	2.8 nM (IC_{50})	5.4 nM (IC_{50})

In Vitro

Fimepinostat is a potent pan-inhibitor of HDAC classes I and II enzymes and observed that its potency against class I HDACs is similar to that of LBH589 and greater than that of SAHA. Fimepinostat is also a potent inhibitor of class I PI3K kinases with an IC50 of 19, 54, and 39 nM for PI3Kα, PI3Kβ, and PI3Kδ, respectively. Fimepinostat markedly induces p21 protein in H460, a non-small cell lung cancer (NSCLC) cell line. Fimepinostat causes the reduction of both p-STAT3 (Y-705) and p-SRC in RPMI-8226 multiple myeloma cells and reduces both phosphorylated and total protein levels of MET and EGFR as well as HER2 and HER3 in H1975 NSCLC cells and BT-474 breast cancer cells, respectively. Fimepinostat induces caspase-3 and -7 activation in HCT-116 colon cancer cells in a dose-dependent manner. Fimepinostat potently inhibits the growth of cancer cells derived from both hematologic and solid tumors. Fimepinostat potently inhibits the proliferation of cells expressing either mutant or wild-type PI3K[1].

In Vivo

Oral administration of Fimepinostat inhibits growth of the Daudi cancer cell xenografts in a dose-dependent manner. Tumor stasis is observed at 100 mg/kg in this model without obvious toxicity. Importantly, in the same model, Fimepinostat achieves better efficacy than GDC-0941, SAHA, or a combination of these 2 compounds given at their maximal tolerated doses (MTD). Furthermore, Fimepinostat causes tumor regression or stasis after intravenous (50 mg/kg) or oral administration (100 mg/kg) in a xenograft tumor model of SU-DHL4 diffuse large B-cell lymphoma (DLBCL) and causes tumor stasis in KRAS-mutant A549 NSCLC cell xenografts[1].

In Vitro:

DMSO : ≥ 50 mg/mL (98.32 mM)

DMF : 5 mg/mL (9.83 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9664 mL	9.8319 mL	19.6637 mL
5 mM	0.3933 mL	1.9664 mL	3.9328 mL
10 mM	0.1966 mL	0.9832 mL	1.9664 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。

Solvent&Solubility	***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→ 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (4.92 mM); Clear solution; Need ultrasonic 此方案可获得 2.5 mg/mL (4.92 mM)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。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (4.92 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.92 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]. Qian C, et al. Cancer network disruption by a single molecule inhibitor targeting both histone deacetylase activity and phosphatidylinositol 3-kinase signaling. Clin Cancer Res. 2012 Aug 1;18(15):4104-13.

实验参考：

Cell Assay	Human cancer cell lines are plated at densities of 5,000 to 10,000 per well in 96-well flat-bottomed plates with the recommended culture medium. The cells are then incubated with compounds (e.g.,Fimepinostat) at various concentrations for 72 hours in culture medium supplemented with 0.5% (v/v) FBS. Growth inhibition is assessed by assay of cellular ATP content using the Perkin-Elmer ATPlite kit[1].
Animal Administration	Mice[1] Six- to 8-week-old female athymic (nude nu/nu CD-1) or severe combined immunodeficient (SCID) mice obtained from Charles River Laboratories are injected subcutaneously with 3 to 20×10^6 cells in a medium suspension of 100 to 200 μL into the right hind flank region. Varying doses of Fimepinostat, standard anticancer agents, or vehicle are administered orally or via tail vein injection as indicated.
Kinase Assay	The activities of classes I and II HDACs are measured using the Color-de-Lys assay system. The activity of PI3K is measured using the ADP-Glo luminescent kinase assay. Recombinant PI3K protein, a complex of N-terminal GST-tagged recombinant full-length human p110 and untagged recombinant full-length human p85, is coexpressed in a baculovirus-infected Sf9 cell expression system[1].
References	[1]. Qian C, et al. Cancer network disruption by a single molecule inhibitor targeting both histone deacetylase activity and phosphatidylinositol 3-kinase signaling. Clin Cancer Res. 2012 Aug 1;18(15):4104-13.