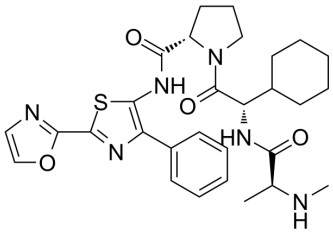
CUDC-427

Cat. No.:	HY-15835
CAS No.:	1446182-94-0
Molecular Formula:	$C_{29}H_{36}N_6O_4S$
Molecular Weight:	564.7
Target:	IAP
Pathway:	Apoptosis

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (88.54 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7709 mL	8.8543 mL	17.7085 mL
5 mM	0.3542 mL	1.7709 mL	3.5417 mL
10 mM	0.1771 mL	0.8854 mL	1.7709 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CUDC-427 is a potent second-generation pan-selective IAP antagonist, used for treatment of various cancers.

In Vitro

GDC-0917 (0.1 nM-10 μM) induces reduction of cIAP1 levels in PBMCs in a concentration-dependent manner showing greater than 80% inhibition at concentrations greater than 0.1 μM (56.5 ng/mL)[1].

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

In Vivo

GDC-0917 (0.08-16.3 mg/kg) exhibits antitumor activity in a dose dependent manner in the MDA-MB-231-X1.1 Breast Cancer Xenograft, and GDC-0917 is well tolerated, with all dose groups experiencing a <11% decrease in mean body weight. GDC-0917 has low to moderate clearance in the mouse (12.0 mL/min/kg), rat (27.0 mL/min/kg), and dog (15.3 mL/min/kg), and high clearance in the monkey (67.6 mL/min/kg). Oral bioavailability is lowest in monkeys compared with other species[1].

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PROTOCOL

Animal Administration [1]

Briefly, 10 million MDA-MB-231-X1.1 breast adenocarcinoma cells resuspended in Hank's balanced salt solution and Matrigel (1:1, v/v) are implanted subcutaneously into the upper right flank of female SCID.bg mice. MDA-MB-231-X1.1 cells are MDA-MB-231 cells that are selected for improved in vivo growth rates. When tumor volumes reach approximately 100-300 mm^3, mice are assigned to treatment groups to get a similar mean tumor size for each treatment group. Treatment groups (n=5 per group) are administered once daily oral doses of vehicle (15% hydroxypropyl-β-cyclodextrin, 20 mM succinic acid in water), 0.08, 0.17, 0.34, 0.68, 1.36, 2.72, 5.43, 10.87, or 16.30 mg/kg of GDC-0917 for 21 days. Tumor volumes are measured in two dimensions (length and width) using Ultra Cal IV calipers. Tumor sizes and body weights are recorded twice weekly, and the mice are regularly observed over the course of the study. Mice are euthanized if their tumor volume exceeds 2000 mm^3 or if their body weight drops by more than 20% of the starting weight.

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

CUSTOMER VALIDATION

- Cell Death Differ. 2020 May;27(5):1569-1587.
- Clin Transl Med. 2022 Jul;12(7):e961.
- Br J Cancer. 2023 Mar 23.

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REFERENCES

[1]. Wong H, et al. Learning and confirming with preclinical studies: modeling and simulation in the discovery of GDC-0917, an inhibitor of apoptosis proteins antagonist. Drug Metab Dispos. 2013 Dec;41(12):2104-13.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA