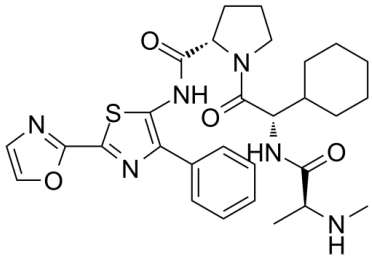
Data Sheet

Product Name:	CUDC-427
Cat. No.:	CS-3392
CAS No.:	1446182-94-0
Molecular Formula:	C29H36N6O4S
Molecular Weight:	564.70
Target:	IAP
Pathway:	Apoptosis
Solubility:	DMSO : ≥ 61 mg/mL (108.02 mM)



BIOLOGICAL ACTIVITY:

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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: CUDC-427 is formulated in 15% hydroxypropyl-β-cyclodextrin, 20 mM succinic acid in water.[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. The following formula is used with Excel version 11.2 to calculate tumor volume (TV): TV (mm^3) = (Length × $Width^2$) ×0.5. 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.

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.

CAIndexNames:

L-Prolinamide, N-methyl-L-alanyl-(2S)-2-cyclohexylglycyl-N-[2-(2-oxazolyl)-4-phenyl-5-thiazolyl]-

SMILES:

O=C([C@H](CCC1)N1C([C@H](C2CCCCC2)NC([C@H](C)NC)=O)=O)NC3=C(C4=CC=CC=C4)N=C(C5=NC=CO5)S3

Caution: Product has not been fully validated for medical applications. For research use only.

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