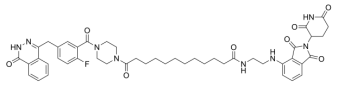
SK-575

Cat. No.:	HY-139156
CAS No.:	2523016-96-6
Molecular Formula:	$C_{47}H_{53}FN_8O_8$
Molecular Weight:	876.97
Target:	PARP; PROTACs
Pathway:	Cell Cycle/DNA Damage; Epigenetics; PROTAC
Storage:	-20°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (114.03 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.1403 mL	5.7014 mL	11.4029 mL
5 mM	0.2281 mL	1.1403 mL	2.2806 mL
10 mM	0.1140 mL	0.5701 mL	1.1403 mL

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

BIOLOGICAL ACTIVITY

Description

SK-575 is a highly potent and specific proteolysis-targeting chimera (PROTAC) degrader of PARP1, with an IC_{50} of 2.30 nM. SK-575 potently inhibits the growth of cancer cells bearing BRCA1/2 mutations[1].

IC_{50} & Target

PARP1
2.30 nM (IC_{50})

In Vitro

SK-575 inhibits cell growth in MDA-MB-436 and Capan-1 cells, with IC_{50} values of 19 ± 6 nM and 56 ± 12 nM, respectively[1].
SK-575 (0-1 μM, 24 h) shows good PARP1 degradation activity in cancer cell lines (MDA-MB-436, Capan-1, and SW620 cells)[1].
SK-575 (0-10 μM, 24 h) effectively induces the formation of γH2AX in MDA-MB-436 and Capan-1 cells in a dose dependent manner[1].

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

Western Blot AnalysisM[1]

Cell Line:	MDA-MB-436, Capan-1, and SW620 cells
Concentration:	10000, 1000, 300, 100, 30, 10, 3, 1, 0.3, 0.1, 0.03, and 0.01 nM

Incubation Time:	24 h
Result:	Showed good PARP1 degradation activity in these cancer cell lines (MDA-MB-436, Capan-1, and SW620 cells), with IC_{50} values of 1.26, 6.72 and 0.509 nM, respectively. Effectively induced the formation of γH2AX in MDA-MB-436 and Capan-1 cells in a dose dependent manner.

In Vivo

SK-575 (mice bearing BRCA2-mutated Capan-1 xenografts, 25 and 50 mg/kg, IP, once daily for 5 days) significantly inhibits the tumor growth in vivo as a single-agent in HR-deficient xenograft models[1].

SK-575 (25 mg/kg, IP, once) achieves sufficient exposure in plasma for over 24 h and effectively induces PARP1 degradation in the SW620 xenograft tumor tissue with the effect persisting for >24 h[1].

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

Animal Model:	Male BALB/c nude mice (bearing xenograft Capan-1 tumors)[1]
Dosage:	25 mg/kg, 50 mg/kg
Administration:	IP, once daily for 5 consecutive days
Result:	Inhibited tumor growth. SK-575 at these doses (25 and 50 mg/kg) were well tolerated, with no mice lethality or significant weight loss observed during the treatment time.

Animal Model:	Female ICR mice (20-23 g, 6-7 week-old, n=3 per group)[1]
Dosage:	25 mg/kg
Administration:	Intraperitoneally, a single dose (Pharmacokinetic Analysis)
Result:	Pharmacokinetic Parameters of SK-575 in female ICR mice[1].

Parameters	mean
T_{max} (h)	0.25
C_{max} (ng/mL)	1843
AUC_{all} (ng/mL⋅h)	5316
AUC_{inf} (ng/mL⋅h)	5363
$t_{1/2}$ (ng/mL)	3.08

REFERENCES

[1]. Cao C, et al. Discovery of SK-575 as a Highly Potent and Efficacious Proteolysis-Targeting Chimera Degrader of PARP1 for Treating Cancers. J Med Chem. 2020 Oct 8;63(19):11012-11033.

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

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