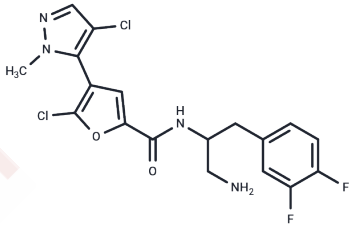
Data Sheet (Cat.No.T6849)

TargetMol

Uprosertib

Chemical Properties



CAS No. : 1047634-65-0

Formula: C18H16Cl2F2N4O2

Molecular Weight: 429.25

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Uprosertib (GSK2141795) is a potent, selective Akt broad-spectrum inhibitor with IC50 values of 180/328/38 nM for Akt1/Akt2/Akt3.
Targets(IC50)	Akt
In vitro	**METHODS**: Lysates of a mixture of K562, COLO205, SKNBE2, and OVCAR8 cells were preincubated with 0, 2.5 nM, 25 nM, 250 nM, 2.5 μM, or 25 μM of the free compound Uprosertib (GSK2141795) for 45 min at 4°C on an end-to-end shaker. Subsequently, lysates were incubated with beads (coupled to Akt probes or kinobads) for 1 h at 4°C to perform qualitative and quantitative experiments. **RESULTS** Uprosertib inhibits kinobead binding. The IC50 value of Akt1 is 180 nM, the IC50 value of Akt2 is 328 nM, and the IC50 value of Akt3 is 38 nM; the KD value of Akt1 is 16 nM, the KD value of Akt2 is 49 nM, and the KD value of Akt3 The value is 5 nM. [1] **METHODS**: HAP1, HAP1 RNF43 KO, and HAP1 PWWP2B KO cells were treated with 10 μM Uprosertib for 48 hours, and the inhibitory effect of Uprosertib was evaluated using MTS assay and the effect on cell line viability was detected. **RESULTS** Uprosertib reduced cell viability in a dose-dependent manner. [2] **METHODS**: HCT116 and LS174T cell lines were treated with uprosertib (1 μM to 15 μM) for 72 h in the presence or absence of lactate (0-20 mM), and biomass was determined using the SRB assay; Cells were treated with uprosertib (5 or 10 μM) for 24 h and apoptosis was measured using the Caspase-Glo 3/7 assay. **RESULTS** Uprosertib induced dose-dependent cytotoxicity in both cell lines; uprosertib induced a dose-dependent increase in caspase-3/7 activation in HCT116 and LS174T cell lines. [3]
In vivo	**METHODS**: Uprosertib (GSK2141795) (10 mg/kg/day, oral) was used to study in vivo efficacy on the growth of MKN45 xenograft models. **RESULTS** Uprosertib significantly inhibited tumor growth at 3 weeks, with 27% inhibition in KMN45 xenografts. [2]
Kinase Assay	Selectivity profiling experiments: The lysates (5 mg of total protein each) are preincubated with 0 (DMSO control), 2.5 nM, 25 nM, 250 nM, 2.5 μM or 25 μM free compound (GSK690693 or GSK2141795) on an end-over-end shaker for 45 min at 4 °C. Subsequently, lysates are incubated with beads (coupled Akt probe or kinobeads) for 1 h at 4 °C, for both qualitative and quantitative experiments. The beads are washed with 1× CP buffer and collected by centrifugation. Bound proteins are eluted with 2× NuPAGE LDS sample buffer, and eluates are reduced and alkylated by 50 mM dithiothreitol and

	55 mM iodoacetamide.
Cell Research	Cell lines are typically grown in RPMI 160 medium containing 10% FBS. Some cell lines are grown in media specified by the vendor. A 3-day proliferation assay using CellTiter-Glo is performed to measure the growth inhibition by the compounds at 0-30 μM. Cell growth is determined relative to untreated (DMSO) controls. EC50's are calculated from inhibition curves using a 4- or 6-parameter fitting algorithm in the Assay Client application.(Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 76 mg/mL (177.05 mM),Sonication is recommended. DMSO: 65 mg/mL (151.43 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3296 mL	11.6482 mL	23.2964 mL
5 mM	0.4659 mL	2.3296 mL	4.6593 mL
10 mM	0.233 mL	1.1648 mL	2.3296 mL
50 mM	0.0466 mL	0.233 mL	0.4659 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Pachl F, et al. Characterization of a chemical affinity probe targeting Akt kinases. J Proteome Res. 2013 Aug 2;12 (8):3792-800.

Bing S, Xiang S, Xia Z, et al.AKT inhibitor Hu7691 induces differentiation of neuroblastoma cells.Acta Pharmaceutica Sinica B.2023

Sohn SH, et al. RNF43 and PWWP2B inhibit cancer cell proliferation and are predictive or prognostic biomarker for FDA-approved drugs in patients with advanced gastric cancer. J Cancer. 2021 Jun 1;12(15):4616-4625.

Chang Y, Wang X, Yang J, et al.Development of an orally bioavailable CDK12/13 degrader and induction of synthetic lethality with AKT pathway inhibition.Cell Reports Medicine.2024

Barnes EME, et al. Lactic acidosis induces resistance to the pan-Akt inhibitor uprosertib in colon cancer cells. Br J Cancer. 2020 Apr;122(9):1298-1308.