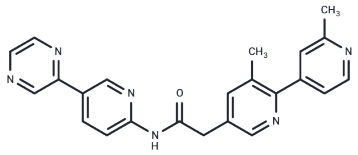
Data Sheet (Cat.No.T2618)

TargetMol
YOUR TARGET MOLECULES

LGK974

Chemical Properties



CAS No. : 1243244-14-5

Formula: C23H20N6O

Molecular Weight: 396.44

Appearance: no data available

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

Biological Description

Description	LGK974 (NVP-LGK974) is an effective and selective PORCN inhibitor and inhibits Wnt signaling (IC50: 0.4 nM) in TM3 cells. It has been used in trials studying the treatment of Metastatic Colorectal Cancer and Squamous Cell Carcinoma, Head And Neck.
Targets(IC50)	Porcupine
In vitro	In both the MMTV-WNT1 mouse model of breast carcinoma and the human head and neck squamous cell carcinoma model (hn30), LGK-974 (3 mg/kg) inhibits the Wnt signaling pathway, leading to tumor regression without affecting mouse body weight. Additionally, LGK-974 (5 mg/kg, twice daily, orally) also suppresses the growth of RNF43-mutant pancreatic tumors (HPAF-II and Capan-2).
In vivo	LGK-974 inhibits a range of tested Wnts, with IC50 values between 0.05 to 2.4 nM. In the PORCN radioligand binding assay, LGK-974 effectively displaces [3H]GNF-1331 with an IC50 of 1 nM and exhibits minimal cytotoxicity at 20 μM. It specifically inhibits the growth of RNF43 mutant cell lines HPAF-II, PaTu 8988S, and Capan-2.
Kinase Assay	Radioligand binding assay: using the aforementioned membrane preps, filtration binding assays are performed. To reduce nonspecific binding, 96-well filtration plates are precoated as suggested by the manufacturer with 0.1% BSA and then washed four times with 0.1% BSA. Membrane preps (50 μg total protein) are incubated in polypropylene 96-well plates with 6.6 nM 3H-GNF-1331 in the presence or absence of a testing compound in binding buffer (50 mM Tris, pH 7.5, 5 mM MgCl2, 1 mM EDTA, 0.1% BSA) plus EDTA-free protease inhibitor mixture in a final volume of 150 μL for 3 h at room temperature. Binding reaction mixtures are then transferred to the precoated 96-well filtration plates, filtered, and washed using a 96-pin FilterMate Harvester. Radioactive signals are obtained using a Microplate Scintillation Counter TopCount. Curve fitting is performed using Prism[1].
Cell Research	Cells are plated in growth medium in a 96-well plate at a density of 6,000–12,000 cells per well and treated with DMSO or 1 μM LGK974. After 3 d, the cells are treated with fresh growth medium containing 20 μM EdU, which is included in the Click-iT EdU Alexa Fluor 488 HCS assay kit, and the plate was incubated for 2 h at 37 °C in a humidi?ed atmosphere containing 5% CO2. Cells are ?xed with ?nal 4% (mass/vol) paraformaldehyde for 30 min, washed with PBS, permeabilized, and stained with 50 μg/mL Hoechst in PBS for 30 min. After wash, the cells are proceeded to EdU detection according to the instruction of Click-iT EdU assay kit. Triplet wells are performed for each condition. (Only for Reference)

Solubility Information

Solubility	DMSO: 73 mg/mL (184.1 mM), Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5224 mL	12.6122 mL	25.2245 mL
5 mM	0.5045 mL	2.5224 mL	5.0449 mL
10 mM	0.2522 mL	1.2612 mL	2.5224 mL
50 mM	0.0504 mL	0.2522 mL	0.5045 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

Zhang W, Li X, Jiang M, et al.SOCS3 deficiency-dependent autophagy repression promote the survival of early-stage myeloid-derived suppressor cells in breast cancer by activating the Wnt/mTOR pathway.Journal of