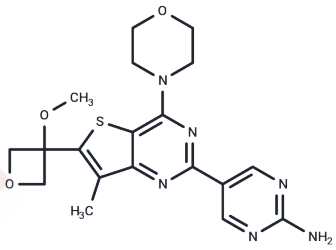
Data Sheet (Cat.No.T6845)

TargetMol

GNE-317

Chemical Properties



CAS No. : 1394076-92-6

Formula: C19H22N6O3S

Molecular Weight: 414.48

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	GNE-317, a PI3K/mTOR inhibitor, can pass through the blood-brain barrier (BBB).
Targets(IC50)	mTOR,PI3K
In vitro	GNE-317, an oxetane derivative synthesized by GDC-0980, is aimed at reducing substrate affinity for efflux transporters. In vitro, GDC-0980 demonstrate similar profiles with GNE-317 in MTS cytotoxicity experiments using the GL261 cell line.
In vivo	Mice, which are i.c. inoculation with GL261-GFP-Luc cells Seven days later,are treated once daily with the maximum tolerated dose of GDC-0980 (7.5 mg/kg), GNE-317 (30 mg/kg), or vehicle. Tumor growth is tracked in GL261 through bioluminescence imaging on a weekly basis. There are no significant differences in GL261 tumor growth among the 3 groups treated by GDC-0980, GNE-317 or vehicle. The data show that the drugs have limited efficacy in inducing cell death in the GL261 cell line. Although GNE-317 has greater delivery and enhanced therapeutic targeting efficacy, it is not effective in the treatment of the GL261 tumor.
Cell Research	Cellular viability assays are set up in a 96-well format with 2000 GL261-GFP-Luc cells plated per well in the culture conditions. GL261, an aggressive C57BL/6J-derived glioma line, is transfected with both green fluorescent protein (GFP) and luciferase (Luc) from separate plasmids.GL261-GFP-Luc cells are cultured in Dulbecco's modified Eagle's medium supplemented with 10% FBS and Penicillin/Streptomycin (100 U/mL) at 5% oxygen, and are selected by 4 mg/mL Puromycin and 4 mg/mL G418. Suspend GNE-317 in DMSO and then diluted with the medium.GL261-GFP-Luc cells are incubated in the presence of drug or vehicle for 48 hours, and viability was assessed by MTS assay. Results were detected using a Synergy Mx automated plate reader,which are set up absorbance at 490 nm and used to determine viability and at 650 nm to account for the background. Numerical values from drug-treated wells are normalized to the values of vehicle-treated wells to yield percent survival.
Animal Research	7-week-old C57BL/6J mice are implanted GL261-GFP-Luc cells. When tumors reach 5e7 photons/s/cm2/sr (radiance), mice are orally administered the maximum tolerated the dose,which is defined as <10% drop in mice bodyweight dose, GDC-0980 for 7.5 mg/kg, GNE-317 for 30 mg/kg or vehicle once daily for 3 days. At 1 or 6 hours after the third dose, mice are euthanized with carbon dioxide and perfused with 30 mL PBS.

Solubility Information

Solubility	DMSO: 12.5 mg/mL (30.16 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.4127 mL	12.0633 mL	24.1266 mL
5 mM	0.4825 mL	2.4127 mL	4.8253 mL
10 mM	0.2413 mL	1.2063 mL	2.4127 mL
50 mM	0.0483 mL	0.2413 mL	0.4825 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Salphati L, et al. Clin Cancer Res. 2012, 18(22):6239-6248

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