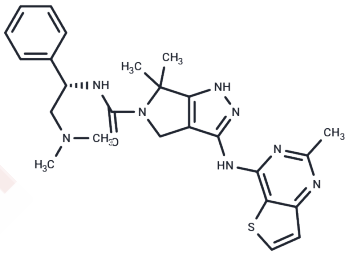
Data Sheet (Cat.No.T6626)

TargetMol

PF-3758309

Chemical Properties



CAS No. : 898044-15-0

Formula: C25H30N8OS

Molecular Weight: 490.62

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	PF-3758309 (PF-03758309) (IC50=1.3 nM), a pyrrolopyrazole inhibitor of PAK4, has effective ATP-competition.
Targets(IC50)	Apoptosis,PAK
In vitro	PF-3758309 (Kd = 2.7 nM), an effective inhibitor of PAK4 （Ki=18.7 nM）, has ATP competition. PF-3758309 (IC50 = 1.3 nM) inhibits phosphorylation of the PAK4 substrate GEF-H1 in cells. In the tumor cell, PF-3758309(IC50 = 4.7 nM) grows in a linesanchorage-independent manner. In HCT116 cells, PF-3758309 inhibits endogenous pGEF-H1 accumulation. In A549 cells, PF-3758309 effectively inhibits cellular proliferation in IC50 of 20 nM and anchorage-independent growth in IC50 of 27 nM.
In vivo	In the HCT116 tumor model, PF-3758309 act as an antiproliferative inducing apoptosis. In the sensitive model, PF-3758309 (EC50=0.4 nM) blocks the growth of multiple human tumor xenografts.
Kinase Assay	In phospho-GEF-H1 cellular assay, TR-293-KDG cells are incubated for 3 hours with PF-3758309. TR-293-KDG cells were captured on an anti-HA antibody-coated plate, which is detected with an anti-phospho-S810-GEF-H1 antibody, and quantified with a horseradish peroxidase-goat anti-rabbit antibody conjugate. TR-293-KDG cells are constructed from HEK293 cells, which is transfected with tetracycline-inducible PAK4-kinase domain (amino acids 291-591) and expressed HA-tagged GEFH1ΔDH (amino acids 210-921).
Cell Research	HEK293T, HCT116, and SKOV3 cells are plated on 384-well plates for 24 hours culture. PF-3758309(~1 μM) is added to the cell culture incubating 72 hours. After drug treatment,cell proliferation and other indicators of metabolism are measured.
Animal Research	Nude mice with Xenograft tumors were orally fed with PF-3758309 （7.5-30 mg/kg BID） dissolved in 0.5% methylcellulose.

Solubility Information

Solubility	DMSO: 150 mg/mL (305.74 mM),Sonication is recommended. Ethanol: 91 mg/mL (185.48 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 3.3 mg/mL (6.73 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0382 mL	10.1912 mL	20.3824 mL
5 mM	0.4076 mL	2.0382 mL	4.0765 mL
10 mM	0.2038 mL	1.0191 mL	2.0382 mL
50 mM	0.0408 mL	0.2038 mL	0.4076 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

Murray BW, et al. Proc Natl Acad Sci U S A, 2010, 107(20), 9446-9451.