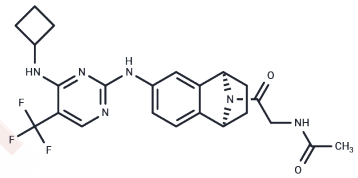
Data Sheet (Cat.No.T6936)

PF-03814735

Chemical Properties



CAS No. : 942487-16-3

Formula: C23H25F3N6O2

Molecular Weight: 474.48

Storage: Store at low temperature
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-03814735 is a novel, potent and reversible inhibitor of Aurora A/B with IC50of 0.8 nM/5 nM, is less potent to Flt3, FAK, TrkA, and minimally active to Met and FGFR1. Phase 1.
Targets(IC50)	FAK,FLT,Aurora Kinase,Trk receptor,VEGFR
In vitro	In intact cells, the inhibitory activity of PF-03814735 on the Aurora1 and Aurora2 kinases reduces levels of phospho-Aurora1 (Thr 232, a sensitive marker of Aurora1 activity, with IC50 ~ 20 nM), phosphohistone H3 (with IC50 ~ 50 nM), and phospho-Aurora2 (with IC50 ~150 nM). PF-03814735 produces a block in cytokinesis, resulting in inhibition of cell proliferation and the formation of polyploid multinucleated cells. [1] A recent research indicates small cell lung cancer (SCLC) and, to a lesser extent, colon cancer lines are very sensitive to PF-03814735. The status of the Myc gene family and retinoblastoma pathway members significantly correlates with the efficacy of PF-03814735. [1]
In vivo	Once-daily oral dosing of ≥20 mg/kg of PF-03814735 for 10 days to mice bearing HCT-116 xenografts resulted in statistically significant and dose-dependent tumor growth inhibition of ≥50% relative to vehicle-treated mice. The inhibition is associated with a reduction in phosphorylated histone H3 levels. Significant single-agent antitumor efficacy is observed in five additional xenograft tumor models, including A2780 ovarian carcinoma, MDA-MB-231 breast carcinoma, colo-205 and SW620 colorectal carcinomas, and HL-60 acute promyelocytic leukemia. [1] In vivo experiments with two SCLC xenograft models confirms the sensitivity of Myc gene-driven models to PF-03814735 and a possible schedule dependence of MYC/c-Myc-driven tumors. [1]
Kinase Assay	Recombinant Kinase Assays: Aurora1 and Aurora2 proteins are produced as full-length His-tag recombinant proteins expressed in insect cells. For the Aurora2 kinase assay, phosphorylation of the substrate peptide by recombinant Aurora2 protein is assessed by a Z'-LYTE assay at 3 to 300 μM ATP and various concentrations of PF-03814735 over 60 minutes, at a substrate peptide concentration of 2 μM (biotinylated LRRWSLG, ×4). Phosphorylation is linear over this time for all conditions. For the Aurora1 kinase assay, phosphorylation of the substrate peptide by recombinant Aurora1 protein is assessed by a scintillation proximity assay in a 96-well plate format in which the incorporation of 33P into the peptide substrate (biotinylated LRRWSLG, ×4) is measured by capturing the peptide on a streptavidin scintillation proximity assay bead.

Cell Research	Cell lines are grown in appropriate media and evaluated after 48 h of exposure to either PF-03814735 or vehicle, followed by cell number determination in a Coulter Counter. Proliferation (as measured by an increase in cell number) is expressed as a percent of untreated controls. To evaluate the PF-03814735 exposure time required for antiproliferative activity, HL-60 cell cultures are cultured in RPMI medium supplemented with 15% heat-inactivated fetal bovine serum and exposed to various PF-03814735 concentrations for 4, 8, 12, 24, and 48 hours, followed by a washout step and incubation with growth media without PF-03814735 for the remainder of the 72-h assay period. Continuous exposure to PF-03814735 for 72 hours is also evaluated. Cell counts are determined by a Coulter Counter.(Only for Reference)

Solubility Information

Solubility	DMSO: 47.5 mg/mL (100.11 mM),Sonication is recommended. Ethanol: 9.5 mg/mL (20.02 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 2 mg/mL (4.22 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	2.1076 mL	10.5379 mL	21.0757 mL
5 mM	0.4215 mL	2.1076 mL	4.2151 mL
10 mM	0.2108 mL	1.0538 mL	2.1076 mL
50 mM	0.0422 mL	0.2108 mL	0.4215 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

Jani JP, et al, Mol Cancer Ther, 2010, 9(4), 883-894.
Hook KE, et al, Mol Cancer Ther, 2012, 11(3), 710-719.

Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481