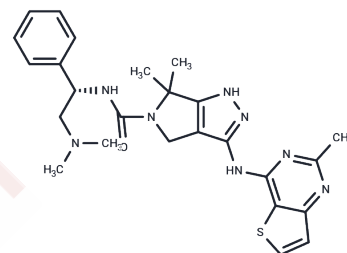


PF-3758309

Chemical Properties

CAS No. : 898044-15-0
 Formula: C₂₅H₃₀N₈O₅
 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) (IC ₅₀ =1.3 nM), a pyrrolopyrazole inhibitor of PAK4, has effective ATP-competition. |
| Targets(IC ₅₀) | Apoptosis,PAK |
| In vitro | PF-3758309 (K _d = 2.7 nM), an effective inhibitor of PAK4 (K _i =18.7 nM) , has ATP competition. PF-3758309 (IC ₅₀ = 1.3 nM) inhibits phosphorylation of the PAK4 substrate GEF-H1 in cells. In the tumor cell, PF-3758309(IC ₅₀ = 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 IC ₅₀ of 20 nM and anchorage-independent growth in IC ₅₀ of 27 nM. |
| In vivo | In the HCT116 tumor model, PF-3758309 act as an antiproliferative inducing apoptosis. In the sensitive model, PF-3758309 (EC ₅₀ =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. H ₂ O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble) |
|------------|---|

A DRUG SCREENING EXPERT

| | |
|---------------------|---|
| In vivo Formulation | 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 3.3 mg/mL (6.73 mM), Sonication is recommended. <i>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.</i> |
|---------------------|---|

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.

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