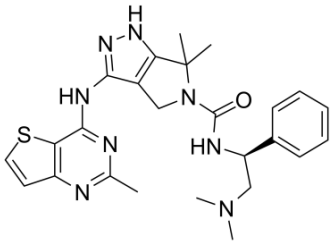
PF-3758309

Cat. No.:	HY-13007
CAS No.:	898044-15-0
Molecular Formula:	$C_{25}H_{30}N_8OS$
Molecular Weight:	490.62
Target:	PAK; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (203.82 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: **10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline**
   Solubility: ≥ 2.5 mg/mL (5.10 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: ≥ 2.5 mg/mL (5.10 mM); Clear solution
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 2.5 mg/mL (5.10 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-3758309 is a potent, orally available, and reversible ATP-competitive inhibitor of **PAK4** (K_d= 2.7 nM; K_i=18.7 nM). PF-3758309 has the expected cellular functions of a PAK4 inhibitor: inhibition of anchorage-independent growth, induction of apoptosis, cytoskeletal remodeling, and inhibition of proliferation[1][2][3].

IC_{50} & Target	PAK4	PAK1	PAK5	PAK6

	18.7 nM (Ki)	13.7 nM (Ki)	18.1 nM (Ki)	17.1 nM (Ki)
	PAK2 190 nM (IC_{50})	PAK3 99 nM (IC_{50})	PAK4 2.7 nM (Kd)	

In Vitro

PF-3758309 has similar enzymatic potency against the kinase domains of the other group B PAKs (PAK5, K_i=18.1 nM; PAK6, K_i=17.1 nM) and group A PAK1 (K_i=13.7 nM), but is less active against the other two group A PAKs (PAK2, IC_{50} =190 nM; PAK3, IC_{50}=99 nM)[1].
In cells, PF-3758309 inhibits phosphorylation of the PAK4 substrate GEF-H1 (IC_{50}=1.3 nM) and anchorage-independent growth of a panel of tumor cell lines (IC_{50}=4.7 nM)[1].
PF-3758309 also inhibits endogenous pGEF-H1 accumulation in HCT116 cells. PF-3758309 potently inhibits cellular proliferation (IC_{50}=20 nM) and anchorage-independent growth (IC_{50}=27 nM) of A549 cells[1].

In Vivo

PF-3758309 (7.5-30 mg/kg; p.o.; twice daily for 9-18 days) results in statistically significant tumor growth inhibition (TGI) in HCT116 and A549 models[1].

Animal Model:	Female nu/nu, CRL breed 6–8 weeks old mice (bearing HCT116 and A549 tumors)[1]
Dosage:	7.5-30 mg/kg
Administration:	Oral administration; twice daily for 9-18 days
Result:	Significant tumor growth inhibition (TGI) in HCT116 and A549 models.

CUSTOMER VALIDATION

- **Science**. 2017 Dec 1;358(6367). pii: eaan4368.
- **Sci Transl Med**. 2018 Jul 18;10(450). pii: eaaq1093.
- **Exp Cell Res**. 2020 Jul 25;112187.
- **Harvard Medical School LINCS LIBRARY**

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REFERENCES

[1]. Murray, Brion W., et al. Small-molecule p21-activated kinase inhibitor PF3758309 is a potent inhibitor of oncogenic signaling and tumor growth. Proceedings of the National Academy of Sciences of the United States of America (2010), 107(20), 9446-9451, S94

[2]. Zhao ZS, et al. Do PAKs make good drug targets? F1000 Biol Rep. 2010 Sep 23;2:70.

[3]. Ryu BJ, et al. PF-3758309, p21-activated kinase 4 inhibitor, suppresses migration and invasion of A549 human lung cancer cells via regulation of CREB, NF-κB, and β-catenin signalings. Mol Cell Biochem. 2014 Apr;389(1-2):69-77.

[4]. Pitts TM, et al. Association of the epithelial-to-mesenchymal transition phenotype with responsiveness to the p21-activated kinase inhibitor, PF-3758309, in colon cancer models. Front Pharmacol. 2013 Mar 28;4:35.

Caution: Product has not been fully validated for medical applications. For research use only.

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