产品名称：**PF-3758309**
产品别名：**PF-3758309**

生物活性：

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.

IC_{50} & Target

PAK4	PAK1	PAK5	PAK6	PAK2	PAK3
18.7 nM (Ki)	13.7 nM (Ki)	18.1 nM (Ki)	17.1 nM (Ki)	190 nM (IC_{50})	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.

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (203.82 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / 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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出

	现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (5.10 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.10 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.10 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.10 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.10 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.10 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.