产品名称：**PF-4708671**
产品别名：**PF-4708671**

生物活性：

Description	PF-4708671 is a potent cell-permeable **S6K1** inhibitor with a **K_i** of 20 nM and **IC_{50}** of 160 nM.

IC_{50} & Target

S6K1	S6K1	S6K2
160 nM (IC_{50})	20 nM (Ki)	65 μM (IC_{50})

In Vitro

PF-4708671 inhibits the activity of full-length S6K1 in vitro with a Ki of 20 nM, and S6K1 isolated from IGF1-stimulated HEK293 cells with an IC50 of 0.16 μM, and only inhibits very weakly the closely related S6K2 isoform (IC50 of 65 μM). PF-4708671 inhibits RSK1 (IC50 of 4.7 μM) and RSK2 (IC50 of 9.2 μM) over 20-fold less potently than S6K1. PF4708671 inhibits MSK1 (IC50 of 0.95 μM) 4-fold more weakly than S6K1[1]. HCT116 cells are treated with (i) vehicle (DMSO), (ii) OSI-906 (5 μM), (iii) PF-4708671 (10 μM), and (iv) OSI-906 (5 μM)+PF-4708671 (10 μM) for various amounts of time. HCT116 cells treated with OSI-906 alone (closed square) or PF4708671 alone (open circle) slightly inhibit cell growth. In contrast, proliferation in HCT116 cells is significantly inhibited after a 2-day treatment with the combination of OSI-906 and PF-4708671 (closed circle). A similar result is also observed when SW480 cells are treated with the combination of OSI-906 and PF-4708671. Colony formation also significantly reduces in OSI-906+PF-4708671-treated cells comparing with vehicle, OSI-906 alone, or PF-4708671 alone treated HCT116 or SW480 cells[2].

In Vivo

The tumor growth rate in mice treated with the combination of OSI-906+PF-4708671 is significantly slower than that of OSI-906 alone (P=0.0189) or PF4708671 alone (P=0.0165) treated mice. The average tumor volume in the OSI-906+PF-4708671-treated mice is approximately 50% of that in mice treated with OSI-906 (P=0.0056) or PF-4708671 alone (P<0.001) at the end of a 15-day treatment[2].

Solvent&Solubility

In Vitro:

DMSO : 33.33 mg/mL (85.37 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5614 mL	12.8070 mL	25.6141 mL
	5 mM	0.5123 mL	2.5614 mL	5.1228 mL
	10 mM	0.2561 mL	1.2807 mL	2.5614 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 (6.40 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.40 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 (6.40 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.40 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 (6.40 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.40 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]. Pearce LR, et al. Characterization of PF-4708671, a novel and highly specific inhibitor of p70 ribosomal S6 kinase (S6K1). Biochem J. 2010 Oct 15;431(2):245-55. [2]. Zhang Y, et al. Inhibition of p70S6K1 Activation by Pdcd4 Overcomes the Resistance to an IGF-1R/IR Inhibitor in Colon Carcinoma Cells. Mol Cancer Ther. 2015 Mar;14(3):799-809.

实验参考：

Cell Assay	GEO, HT29, SW480, and HCT116 cells are used. The effects of OSI-906 or the combination of OSI-906 and PF-4708671 on cell proliferation is determined with XTT and clonogenic assays. XTT assays are performed using the Cell Proliferation Kit II (XTT). For clonogenic assays, cells (1×103 cells/well) are seeded on a 6-well plate and subsequently treated with drugs (OSI-906 5 μM, PF-4708671 10 μM). After 1 week of incubation, cells are stained with 1% crystal violet, and the number of colonies is counted and recorded[2].
Animal Administration	Mice[2] Five- to 6-week-old female athymic nude mice (Hsd:Athymic Nude-Foxn1nu) are randomly assigned to the following groups (5 mice/group). For injection of HT29-L and HT29-P cells, mice are treated with vehicle (25 mM tartaric acid) or OSI-906 (30 mg/kg) for 12 days. For injection of HCT116 cells, mice are treated with (i) vehicle (25 mM tartaric acid); (ii) OSI-906 alone (30 mg/kg); (iii) PF-4708671 alone (60 mg/kg); and (iv) OSI-906 (30 mg/kg)+PF-4708671 (60 mg/kg) and treated with drugs orally for 14 days. Vehicle and OSI-906 are given once per day and PF-4708671 is given once every other day. Twenty-four hours after the last treatment, the mice are sacrificed and the tumor weights were measured[2].
References	[1]. Pearce LR, et al. Characterization of PF-4708671, a novel and highly specific inhibitor of p70 ribosomal S6 kinase (S6K1). Biochem J. 2010 Oct 15;431(2):245-55. [2]. Zhang Y, et al. Inhibition of p70S6K1 Activation by Pdcd4 Overcomes the Resistance to an IGF-1R/IR Inhibitor in Colon Carcinoma Cells. Mol Cancer Ther. 2015 Mar;14(3):799-809.