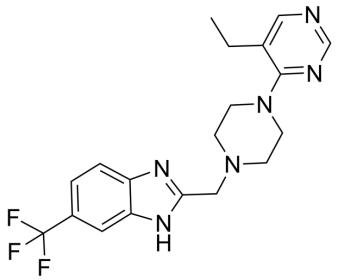
PF-4708671

Cat. No.:	HY-15773
CAS No.:	1255517-76-0
Molecular Formula:	$C_{19}H_{21}F_3N_6$
Molecular Weight:	390.41
Target:	Ribosomal S6 Kinase (RSK); Autophagy
Pathway:	MAPK/ERK Pathway; Autophagy
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 : 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

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 (6.40 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.40 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.40 mM); Clear solution

BIOLOGICAL ACTIVITY

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 K_i of 20 nM, and S6K1 isolated from IGF1-stimulated HEK293 cells with an IC_{50} of 0.16 μM, and only inhibits very weakly the closely related S6K2 isoform (IC_{50} of 65 μM). PF-

	4708671 inhibits RSK1 (IC_{50} of 4.7 μM) and RSK2 (IC_{50} of 9.2 μM) over 20-fold less potently than S6K1. PF4708671 inhibits MSK1 (IC_{50} 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	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 (1×10^3 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Discov. 2022 Jun 8;candisc.1672.2021.
- J Infect. 2019 Sep;79(3):262-276.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cell Rep. 2021 Jun 22;35(12):109277.
- Free Radic Biol Med. 2022 Dec 7;194:184-198.

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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.

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