产品名称：**PF-4989216**
产品别名：**PF-4989216**

生物活性：

Description	PF-4989216 is a potent and selective **PI3Kα** inhibitor with a **K_i** of 0.6 nM.

IC_{50} & Target	PI3Kα	mTOR
	0.6 nM (Ki)	1440 nM (Ki)

In Vitro	PF-4989216 (Compound 10) has excellent PI3Kα Ki (0.6 nM), good cellular potency (S473 IC50=79 nM), and good selectivity against mTOR (mTOR Ki=1440 nM). PF-4989216 has PI3Kα Ki less than 1 nM and mTOR Ki more than 1 μM. PF-4989216 also has excellent selectivity over 40 other kinases, and no major CYP inhibitions are observed. Less than 30% inhibition is observed in 1A2, 2C9, 2D6, and 3A4 CYP enzymes at 3 μM[1]. The toxicity of PF-4989216 in several drug-sensitive and MDR cancer cell lines, including cells overexpressing ABCB1 or ABCG2, and in HEK293 cells transfected with human ABCB1 or ABCG2 is determined. PF-4989216 inhibits human colon carcinoma S1 cell line and ABCG2-overexpressing subline S1-M1-80 with IC50s of 1.11±0.09 and 6.79±1.00 uM, respectively. PF-4989216 inhibits human breast carcinoma MCF-7 and ABCG2-overexpressing sublines MCF7-FLV1000 and MCF7-AdVp3000 IC50s of 2.30±0.68, 23.26±2.94 and 62.57±5.46 uM, respectively. PF-4989216 inhibits pcDNA-HEK293, ABCB1-transected MDR19-HEK293, ABCG2-tranfected R482-HEK293 cells with IC50s of 0.44±0.05, 0.38±0.06 and 5.05±0.89 uM, respectively[2].
In Vivo	PF-4989216 (Compound 10) is dosed orally in our in vivo antitumor model, PI3K driven NCI-H1975 xenograft tumors. PF-4989216 demonstrates dose responsive tumor growth inhibitory activity from 25 to 200 mg/kg in QD oral dosing[1].

Solvent&Solubility

In Vitro:

DMSO： ≥ 29 mg/mL (76.24 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6288 mL	13.1441 mL	26.2881 mL
	5 mM	0.5258 mL	2.6288 mL	5.2576 mL
	10 mM	0.2629 mL	1.3144 mL	2.6288 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 (6.57 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.57 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% corn oil Solubility: ≥ 2.5 mg/mL (6.57 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.57 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]. Liu KK, et al. Highly Selective and Potent Thiophenes as PI3K Inhibitors with Oral Antitumor Activity. ACS Med Chem Lett. 2011 Sep 19;2(11):809-813.

实验参考：

Cell Assay	MTT and CCK-8 assays are performed to determine the general sensitivities of cells to the tested drugs. The human colon carcinoma S1 cell line and ABCG2-overexpressing subline S1-M1-80 are treated with PF-4989216 (0.1, 1 and 10 μM). The human breast carcinoma MCF-7 and ABCG2-overexpressing sublines MCF7-FLV1000 and MCF7-AdVp3000 are treated with PF-4989216 (0.1, 1, 10 and 100 μM).The parental HEK293 and ABCG2-tranfected R482-HEK293 cells are treated with PF-4989216 (0.01, 0.1, 1 and 10 μM). For the reversal of cytotoxicity assays, PF-4989216 or Ko143 or Lapatinib at a nontoxic concentration is added into the cytotoxicity assay, and the extent of reversal is then calculated[2].
Animal Administration	Mice[1] For animal studies, 6-8 week old nu/nu athymic female mice are used. Tumors are established by injecting 2×10^6 cells suspended 1:1 (v/v) with reconstituted basement membrane. For tumor growth inhibition studies, mice with established tumors of ~150 mm^3 are randomized. PF-4989216 (Compound 10) is dosed orally (25, 50, 100 and 200 mg/kg) in a mouse PI3K driven NCI-H1975 xenograft tumor model. Tumor dimensions are measured with vernier calipers, and tumor volumes are calculated. Tumor growth inhibition percentage (TGI %) is calculated.
References	[1]. Liu KK, et al. Highly Selective and Potent Thiophenes as PI3K Inhibitors with Oral Antitumor Activity. ACS Med Chem Lett. 2011 Sep 19;2(11):809-813.