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产品名称：PF-04217903
产品别名：PF-04217903

生物活性：

Description

PF-04217903 is a selective ATP-competitive c-Met inhibitor with IC50 of 4.8 nM, susceptible to oncogenic mutations (no activity to Y1230C mutant). IC50 value: 4.8 nM [1] Target: in vitro: Being more selective than staurosporine or PF-02341066, PF-04217903 displays >1000-fold selectivity for c-Met over a panel of 208 kinases, although more susceptible to oncogenic mutations of c-Met that attenuate potency than PF-02341066. In addition to WT c-Met, PF-04217903 displays similar potency to inhibit the activity of c-Met-H1094R, c-Met-R988C, and c-Met-T1010I with IC50 of 3.1 nM, 6.4 nM, and 6.7 nM, respectively, but has no inhibitory activity against c-Met-Y1230C with IC50 of >10 μM [1]. PF-04217903 in combination with sunitinib significantly inhibits endothelial cells, but not the tumor cells B16F1, Tib6, EL4, and LLC [2] PF-04217903 significantly inhibits the clonogenic growth of LXFA 526L and LXFA 1647L with IC50 values of 16 nM, and 13 nM, respectively, yielding an additive effect when in combination with cetuximab [3]. in vivo: Although unable to inhibit tumor growth in the sunitinib-sensitive B16F1 and Tib6 tumor models, the combination of PF-04217903 and sunitinib significantly inhibits tumor growth in sunitinib-resistant EL4, and LLC tumor models compared with sunitinib or PF-04217903 alone by significantly blocking vascular expansion, indicating a functional role for HGF/c-Met axis in the sunitinib-resistant tumors [2].

Solvent&Solubility

In Vitro:

Ethanol : < 1 mg/mL (insoluble)

DMSO : 20 mg/mL (**53.71 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6854 mL	13.4271 mL	26.8543 mL
5 mM	0.5371 mL	2.6854 mL	5.3709 mL
10 mM	0.2685 mL	1.3427 mL	2.6854 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 mg/mL (5.37 mM); Suspended solution; Need ultrasonic

此方案可获得 2 mg/mL (5.37 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

以 1 mL 工作液为例，取 100 μL 20.0 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 mg/mL (5.37 mM); Suspended solution; Need ultrasonic 此方案可获得 2 mg/mL (5.37 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 20.0 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 mg/mL (5.37 mM); Clear solution 此方案可获得 ≥ 2 mg/mL (5.37 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 20.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Timofeevski SL, et al. Enzymatic characterization of c-Met receptor tyrosine kinase oncogenic mutants and kinetic studies with aminopyridine and triazolopyrazine inhibitors. Biochemistry, 2009, 48(23), 5339-5349. [2]. Shojaei F, et al. HGF/c-Met acts as an alternative angiogenic pathway in sunitinib-resistant tumors. Cancer Res, 2010, 70(24), 10090-10100. [3]. Krumbach R, et al. Primary resistance to cetuximab in a panel of patient-derived tumour xenograft models: activation of MET as one mechanism for drug resistance. Eur J Cancer, 2011, 47(8), 1231-1243.