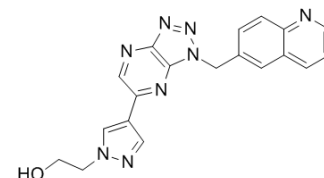


PF-04217903

Cat. No.:	HY-12017		
CAS No.:	956905-27-4		
Molecular Formula:	C ₁₉ H ₁₆ N ₈ O		
Molecular Weight:	372.38		
Target:	c-Met/HGFR		
Pathway:	Protein Tyrosine Kinase/RTK		
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 : 20 mg/mL (53.71 mM; Need ultrasonic)
Ethanol : < 1 mg/mL (insoluble)

	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: 2 mg/mL (5.37 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: 2 mg/mL (5.37 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2 mg/mL (5.37 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-04217903 is a potent ATP-competitive c-Met kinase inhibitor with K_i of 4.8 nM for human c-Met. PF-04217903 shows more than 1,000-fold selectivity relative to 208 kinases. Antiangiogenic properties^{[1][2]}.

IC₅₀ & Target

Ki: 4.8 nM (human c-Met)^[1]

In Vitro

PF-04217903 (0.1-10000 nM; 48-72 hours) inhibits proliferation of c-Met-amplified human GTL-16 gastric carcinoma and

H1993 NSCLC cells with IC₅₀ values of 12 and 30 nM, respectively^[1].
 PF-04217903 (1.5-3333 nM; 48 hours) induces apoptosis of GTL-16 cells (IC₅₀=31 nM)^[1].
 PF-04217903 also inhibits HGF-mediated cell migration and Matrigel invasion in several c-Met-overexpressing tumor cell lines such as human NCI-H441 lung carcinoma and HT29 colon carcinoma with IC₅₀ values comparable with those for inhibition of c-Met phosphorylation in these cell lines (IC₅₀=7-12.5 nM)^[1]. 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^[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay^[1]

Cell Line:	GTL-16, H1993 cells
Concentration:	0.1, 1, 10, 100, 1000, 10000 nM
Incubation Time:	48-72 hours
Result:	Inhibited proliferation of c-Met-amplified human GTL-16 gastric carcinoma and H1993 NSCLC cells with IC ₅₀ values of 12 and 30 nM, respectively.

Apoptosis Analysis^[1]

Cell Line:	GTL-16 cells
Concentration:	1.5-3333 nM
Incubation Time:	48 hours
Result:	Induced apoptosis of GTL-16 cells (IC ₅₀ =31 nM).

In Vivo

PF-04217903 (1-30 mg/kg; p.o.; daily for 16 days) shows dose-dependent tumor growth inhibition, which correlated with the inhibition in c-Met phosphorylation in these tumors^[1].

PF-04217903 (5-50 mg/kg, p.o.; once daily for 3 days) dose dependently inhibits c-Met, Gab-1, Erk1/2, and AKT phosphorylation and induced apoptosis (cleaved caspase-3) in U87MG xenograft tumors at all dose levels. PF-04217903 phenolsulfonate shows a significant dose-dependent reduction of human IL-8 levels in both the U87MG and GTL-16 models and decreases human VEGFA levels in the GTL-16 model. PF-04217903 strongly induces phospho-PDGFRβ levels in U87MG xenograft tumors^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female nu/nu mice (GTL-16 xenograft model) ^[1]
Dosage:	1, 3, 10, 30 mg/kg
Administration:	Oral; daily for 16 days
Result:	Showed dose-dependent tumor growth inhibition, and was correlated with the inhibition in c-Met phosphorylation in these tumors.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Harvard Medical School LINCS LIBRARY

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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]. Zou HY, et al. Sensitivity of selected human tumor models to PF-04217903, a novel selective c-Met kinase inhibitor. *Mol Cancer Ther*. 2012 Apr;11(4):1036-47.
- [3]. Cui JJ, et al. Discovery of a novel class of exquisitely selective mesenchymal-epithelial transition factor (c-MET) protein kinase inhibitors and identification of the clinical candidate 2-(4-(1-(quinolin-6-ylmethyl)-1H-[1,2,3]triazolo[4,5-b]pyrazin-6-yl)-1H-pyrazol-1-yl)ethanol (PF-04217903) for the treatment of cancer. *J Med Chem*. 2012 Sep 27;55(18):8091-109.
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Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA