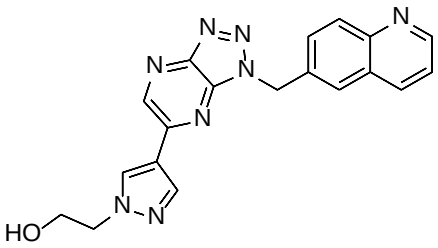
Product data sheet

MedKoo Cat#: 202221 Name: PF-04217903 CAS#: 956905-27-4 (free base) Chemical Formula: $C_{19}H_{16}N_8O$ Exact Mass: 372.1447 Molecular Weight: 372.38	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
PF-04217903 is a MET tyrosine kinase inhibitor, is also a n orally bioavailabe, small-molecule tyrosine kinase inhibitor of the proto-oncogene c-Met (hepatocyte growth factor receptor [HGFR]) with potential antineoplastic activity. c-Met inhibitor PF-04217903 selectively binds to and inhibits c-Met, disrupting the c-Met signaling pathway, which may result in the inhibition of tumor cell growth, migration and invasion of tumor cells, and the induction of death in tumor cells expressing c-Met.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	5.0	13.4

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.69 mL	13.43 mL	26.85 mL
5 mM	0.54 mL	2.69 mL	5.37 mL
10 mM	0.27 mL	1.34 mL	2.69 mL
50 mM	0.05 mL	0.27 mL	0.54 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Zou HY, Li Q, Lee JH, Arango ME, Burgess K, Qiu M, Engstrom LD, Yamazaki S, Parker M, Timofeevski S, Cui JJ, McTigue M, Los G, Bender SL, Smeal T, Christensen JG. 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. doi: 10.1158/1535-7163.MCT-11-0839. Epub 2012 Mar 2. PMID: 22389468.

In vivo study

1. Zou HY, Li Q, Lee JH, Arango ME, Burgess K, Qiu M, Engstrom LD, Yamazaki S, Parker M, Timofeevski S, Cui JJ, McTigue M, Los G, Bender SL, Smeal T, Christensen JG. 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. doi: 10.1158/1535-7163.MCT-11-0839. Epub 2012 Mar 2. PMID: 22389468.

7. Bioactivity
Biological target: PF-04217903 is a c-Met kinase inhibitor with a Ki of 4.8 nM for human c-Met.

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In vitro activity

The antiangiogenic activity of PF-04217903 was evaluated in vitro. PF-04217903 inhibited HGF-stimulated c-Met phosphorylation in HUVECs with an IC50 value of 4.6 nmol/L (Supplementary Table S1). In endothelial cell functional assays, PF-04217903 inhibited HGF-mediated HUVEC survival (IC50 = 12 nmol/L), Matrigel invasion (IC50 = 27 nmol/L), and induced HUVEC apoptosis (IC50 = 7 nmol/L; Table 1).

Reference: Mol Cancer Ther. 2012 Apr;11(4):1036-47. https://mct.aacrjournals.org/content/11/4/1036.long

In vivo activity

PF-04217903 showed marked antitumor activity in tumor models harboring either MET gene amplification or a hepatocyte growth factor (HGF)/c-Met autocrine loop at well-tolerated dose levels in vivo. Antitumor efficacy of PF-04217903 was dose-dependent and showed a strong correlation with inhibition of c-Met phosphorylation, downstream signaling, and tumor cell proliferation/survival. Furthermore, PF-04217903 strongly induced phospho-PDGFRβ (platelet-derived growth factor receptor) levels in U87MG xenograft tumors, indicating a possible oncogene switching mechanism in tumor cell signaling as a potential resistance mechanism that might compromise tumor responses to c-Met inhibitors.

Reference: Mol Cancer Ther. 2012 Apr;11(4):1036-47. https://mct.aacrjournals.org/content/11/4/1036.long