# PF-04217903 phenolsulfonate

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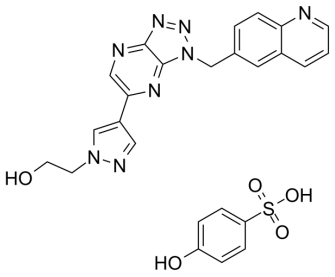
| **Cat. No.:** | HY-12017B |
| **CAS No.:** | 1159490-85-3 |
| **Molecular Formula:** | $C_{25}H_{22}N_8O_5S$ |
| **Molecular Weight:** | 546.56 |
| **Target:** | c-Met/HGFR |
| **Pathway:** | Protein Tyrosine Kinase/RTK |
| **Storage:** | Please store the product under the recommended conditions in the Certificate of Analysis. |



## BIOLOGICAL ACTIVITY

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| **Description** | PF-04217903 phenolsulfonate is a potent ATP-competitive c-Met kinase inhibitor with $K_i$ of 4.8 nM for human c-Met. PF-04217903 phenolsulfonate shows more than 1,000-fold selectivity relative to 208 kinases. Antiangiogenic properties[1][2]. |
| **$IC_{50}$ & Target** | Ki: 4.8 nM (human c-Met)[1] |
| **In Vitro** | PF-04217903 phenolsulfonate (0.1-10000 nM; 48-72 hours) inhibits proliferation of c-Met–amplified human GTL-16 gastric carcinoma and H1993 NSCLC cells with $IC_{50}$ values of 12 and 30 nM, respectively[1].<br>PF-04217903 phenolsulfonate (1.5-3333 nM; 48 hours) induces apoptosis of GTL-16 cells ($IC_{50}$=31 nM)[1].<br>PF-04217903 phenolsulfonate 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 $IC_{50}$ values comparable with those for inhibition of c-Met phosphorylation in these cell lines ($IC_{50}$=7-12.5 nM)[1].<br>PF-04217903 phenolsulfonate displays similar potency to inhibit the activity of c-Met-H1094R, c-Met-R988C, and c-Met-T1010I with $IC_{50}$ of 3.1 nM, 6.4 nM, and 6.7 nM, respectively. PF-04217903 phenolsulfonate has no inhibitory activity against c-Met-Y1230C with $IC_{50}$ of >10 μM[3].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

Cell Viability Assay[1]

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| 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]

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| Cell Line: | GTL-16 cells |
| Concentration: | 1.5-3333 nM |
| Incubation Time: | 48 hours |
| Result: | Induced apoptosis of GTL-16 cells. |

**In Vivo**

PF-04217903 phenolsulfonate (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 phenolsulfonate (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 phenolsulfonate 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.

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| 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]. 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.

[2]. 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.

[3]. Timofeevski SL, et al. Enzymatic characterization of c-Met receptor tyrosine kinase oncogenic mutants and kinetic studies with aminopyridine and triazolopyrazine inhibitors. Biochemistry. 2009 Jun 16;48(23):5339-49.





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