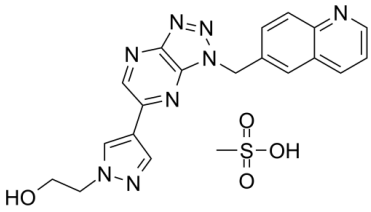
Data Sheet

Product Name:	PF-04217903 (methanesulfonate)
Cat. No.:	CS-0845
CAS No.:	956906-93-7
Molecular Formula:	C20H20N8O4S
Molecular Weight:	468.49
Target:	c-Met/HGFR
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : 50 mg/mL (106.73 mM; Need ultrasonic); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

PF-04217903 methanesulfonate 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: c-Met 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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell assay [2] Cell lines, including B16F1, Tib6, EL4, and LLC, and endothelial cells, HUVECs and C166, were seeded at 104 cells in each well of 24-well tissue culture–treated plates. Cells were grown in the standard media as described earlier. Cells were treated with different concentrations (2, 0.2, and 0.02 μmol/L) of sunitinib, PF-04217903, and combination of both compounds for 4 days. Efficacy of the compounds was measured by counting cells in a Coulter counter machine (BD Biosciences). Similar approach was applied to evaluate the role of HGF or VEGF on cell proliferation, using 3 different concentrations (10, 100, and 200 ng/mL) of each ligand.

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.

CAIndexNames:

1H-Pyrazole-1-ethanol, 4-[1-(6-quinolinylmethyl)-1H-1,2,3-triazolo[4,5-b]pyrazin-6-yl]-, methanesulfonate (1:1)

SMILES:

OCCN1N=CC(C2=NC3=C(N=C2)N=NN3CC4=CC5=CC=CN=C5C=C4)=C1.CS(=O)(O)=O

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

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