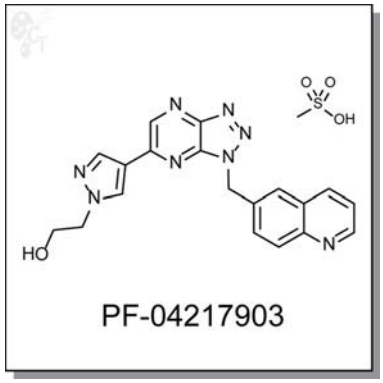
Cellagen Technology

Product Specification Sheet

Product Name: PF-04217903

Catalog Number: C7042



Technical information:

Chemical Formula:	$C_{20}H_{20}N_8O_4S$
CAS #:	956906-93-7
Molecular Weight:	468.49
Purity:	> 98%
Appearance:	White solid
Solubility:	Soluble in DMSO up to 15 mM
Chemical Name:	2-(4-(3-(quinolin-6-ylmethyl)-3H-[1,2,3]triazolo[4,5-b]pyrazin-5-yl)-1H-pyrazol-1-yl)ethanol mesylate
Storage:	Store solid powder at 4°C desiccated; Store DMSO solution at -20°C.
Shelf Life:	In the unopened package, powder is stable for 1 year and DMSO solution is stable for 6 months under proper storage condition.

Handling:

- To make 10 mM stock solution, add 0.213mL of DMSO for each mg of PF-04217903.
- For DMSO solution, briefly spin the vial at 500 rpm in a 50 mL conical tube to ensure maximum sample recovery.

Biological Activity:

PF-04217903 is a triazolopyrazine-based, ATP-competitive inhibitor of c-Met with Ki and cellular IC50 potency of 4 nM and 5 nM, respectively. [1] In a broad panell of over 200 kinases, PF-04217903 showed >1000-fold selectivity for c-Met. For c-Met mutations, PF-04217903 exhibited activities of 6.4 nM, 6.7 nM, and 3.1 nM for endogenous c-Met-R988C, endogenous C-Met-T1010I, and entineered c-Met-H1094R, respectively. [3]

Additionally, PF-04217903 inhibited proliferation, cell survival, migration/invasion in MET-amplified cell lines in vitro and was efficacious in tumor models with either MET gene amplification or hepatocyte growth factor (HGF)/c-Met autocrine loop in vivo. [2, 4] Efficacy was dose-dependent and correlated with inhibition of c-Met phosphorylation and downstream signaling.

Due to its exquisite selectivity profile, PF-04217903 can be considered as a powerful tool in probing c-Met catalytic activity in preclinical models for cancer progression.

Reference:

1. Cui 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, 55, 8091-8109. Pubmed ID: 22924734
2. Zou et al., Sensitivity of selected human tumor models to PF-04217903, a novel selective c-Met kinase inhibitor. Mol. Cancer Ther. 2012, 11, 1036-1047. Pubmed ID: 22389468
3. Timofeevski et al., Enzymatic characterization of c-Met receptor tyrosine kinase oncogenic mutants and kinetic studies with aminopyridine and triazolopyrazine inhibitors. Biochemistry, 2009, 48, 5339-5349. Pubmed ID: 19459657
4. Shojaei et al., HGF/c-Met acts as an alternative angiogenic pathway in sunitinib-resistant tumors. Cancer Res. 2010, 70, 10090-10100. Pubmed ID: 20952508

To reorder: http://www.cellagentech.com/PF-04217903/

For Technical Support: technical@cellagentech.com

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