

Product Data Sheet

Product Name: PF-04217903

Cat. No.: GC12729

Chemical Properties

Cas. No. 956905-27-4

Chemical Name 2-[4-[3-(quinolin-6-ylmethyl)triazolo[4,5-b]pyrazin-5-yl]pyrazol-1-yl]ethanol

SMILES C1=CC2=C(C=CC(=C2)CN3C4=NC(=CN=C4N=N3)C5=CN(N=C5)CCO)N=C1

Formula $C_{19}H_{16}N_8O$

M.Wt 372.38

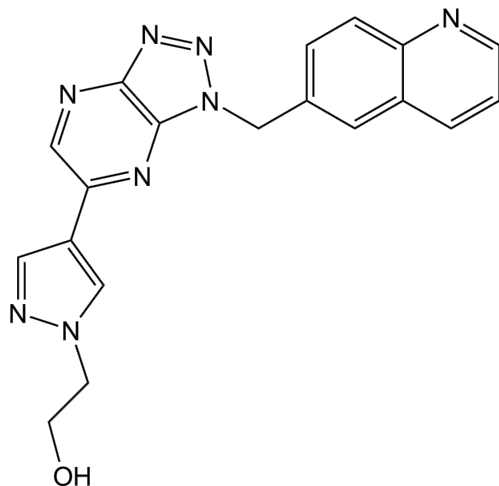
Solubility $\geq 18.6\text{mg/mL}$ in DMSO

Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Background

PF-04217903 is an ATP-competitive small-molecule inhibitor of c-Met kinase with K_i value of 4.8 nM [1].

The c-Met kinase is a kind of receptor tyrosine kinases (RTK) and plays critical roles in embryonic development and wound healing. Activation of c-Met by the exclusive ligand hepatocyte growth factor

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

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(HGF) triggers a series of biological responses that collectively give rise to the invasive growth. In cancers, abnormal activation of c-METs correlates with tumor growth, formation of new blood vessels and subsequently poor prognosis. PF-04217903 is a highly selective inhibitor of c-Met. It showed antitumor activity in tumor models where c-Met is activated by mechanisms including c-Met gene amplification, HGF/c-Met autocrine loop formation or c-Met overexpression [1].

PF-04217903 showed more than 1000-fold greater selectivity against c-Met kinase over 150 other kinases. When evaluated in a panel of human tumor and endothelial cell lines such as GTL-16, H1993 and HT29 cells, PF-04217903 showed inhibition of c-Met with a mean IC₅₀ value of 7.3 nM. PF-04217903 was also found to inhibit some mutant c-Met including R988C (IC₅₀ value of 6.4 nM), V1092I (IC₅₀ value of 16 nM), H1094R (IC₅₀ value of 3.1 nM), M1250T (IC₅₀ value of 24 nM) and T11010I (IC₅₀ value of 6.7 nM). Besides that, PF-04217903 suppressed proliferation of c-Met-amplified GTL-16 and H1993 cells with IC₅₀ values of 12 and 30 nM, respectively. It induced apoptosis in GTL-16 cells [1 and 2].

In mice bearing injected GTL-16 tumors, administration of PF-04217903 showed dose-dependent c-Met phosphorylation inhibition and antitumor efficacy. It inhibited the phosphorylation of c-Met with EC₅₀ value of 10 nM and suppressed tumor growth with EC₅₀ value of 13 nM. Moreover, PF-04217903 was found to affect the downstream signal transduction of c-Met such as AKT, STAT5 and Gab-1 [1].

References:

- [1] Zou H Y, Li Q, Lee J H, et al. Sensitivity of selected human tumor models to PF-04217903, a novel selective c-Met kinase inhibitor. *Molecular cancer therapeutics*, 2012, 11(4): 1036-1047.
- [2] Cui J J, McTigue M, Nambu M, 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)-1 H-[1, 2, 3] triazolo [4, 5-b] pyrazin-6-yl)-1 H-pyrazol-1-yl) ethanol (PF-04217903) for the Treatment of Cancer. *Journal of medicinal chemistry*, 2012, 55(18): 8091-8109.

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