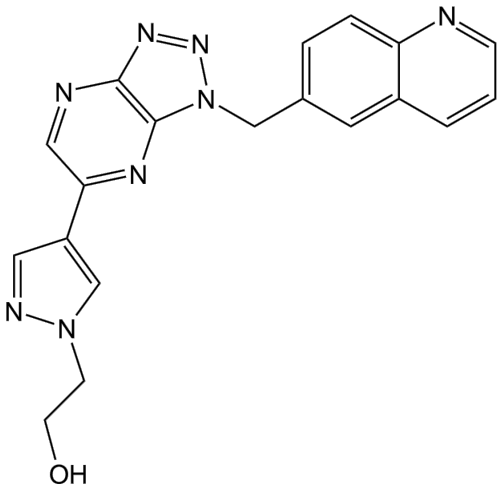
Product Data Sheet

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	≥ 18.6mg/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 Ki 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

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(HGF) triggers a serious 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 H1993cells 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.

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