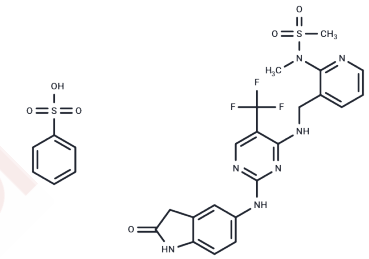
Data Sheet (Cat.No.T6177)

TargetMol

PF-562271 besylate

Chemical Properties



CAS No. : 939791-38-5

Formula: C21H20F3N7O3S·C6H6O3S

Molecular Weight: 665.66

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	PF-562271 besylate (PF-00562271 Besylate) is a potent, ATP-competitive, reversible inhibitor of FAK with IC50 of 1.5 nM, ~10-fold less potent for Pyk2 than FAK and >100-fold selectivity against other protein kinases, except for some CDKs.
Targets(IC50)	FAK,PYK2,CDK
In vitro	PF-562271 shows the selective inhibitory effects on FAK and Pyk2 tyrosine kinase activity with IC50 of 1.5 nM and 14 nM, respectively. And in cell-based assays, the IC50 of PF-562271 is shown to be 5 nM for FAK, which is more selective compared to other kinase targets. [1] In 2 dimensional (2D) cultures, PF-562271 results in a dose-dependent cell proliferation inhibition in FAK WT, FAK?/? and FAK kinase-deficient (KD) cells with IC50 of 3.3 μM, 2.08 μM and 2.01 μM, respectively. [2]
In vivo	In several human s.c. xenograft models, PF-562271 exhibits dose-dependent tumor growth inhibition, and produces maximum tumor inhibition for PC-3M, BT474, BxPc3, and LoVo ranging from 78% to 94% inhibition at doses of 25 to 50 mg/kg twice daily, without weight loss, morbidity, or death. [1] PF-562271 (25 mg/kg by p.o.) leads to a significant decrease in tumor progression in both subcutaneous and bone metastasis PC3M-luc-C6 xenograft models. [3] In a Huh7.5 hepatocellular carcinoma xenograft model, combination therapy of sunitinib and PF-562271 targets angiogenesis and tumor aggressiveness, and produces more significant anti-tumor effect than single agent by blocking tumor growth and impacting the ability of the tumor to recover upon withdrawal of the therapy. [4]
Kinase Assay	Recombinant kinase assay and enzyme kinetics : Briefly, purified-activated FAK kinase domain (amino acid 410-689) is reacted with 50 μM ATP and 10 μg per well of a random peptide polymer of Glu and Tyr, p(Glu/Tyr), in kinase buffer [50 mM HEPES (pH 7.5), 125 mM NaCl, and 48 mM MgCl2] for 15 minutes. Phosphorylation of p(Glu/Tyr) is challenged with serially diluted PF-562271 at 1/2-Log concentrations starting at a top concentration of 1 μM. Each concentration is tested in triplicate. Phosphorylation of p(Glu/Tyr) is detected with a general antiphospho-tyrosine (PY20) antibody followed by horseradish peroxidase (HRP)-conjugated goat anti-mouse IgG antibody. HRP substrate is added, and absorbance readings at 450 nm are obtained after addition of stop solution (2 M H2SO4). IC50 values are determined using the Hill-Slope Model. Broad kinase selectivity profiling is performed in house and by using the KinaseProfiler Selectivity Screening Service available through UpState Biotechnology.

Cell Research	Cells are plated for 48 hours before addition of PF-562271. After 3 days cells are fixed by addition of ice cold 25% trichloroacetic acid (TCA) solution prior to staining with Sulforhodamine B (SRB) dye solution. Plates are washed with 1% glacial acetic acid, air-dried and resuspended in 10 mM Tris buffer, pH 10.5 before reading absorbance at 540 nm. Curve fitting and generation of IC50 values is carried out using GraphPad Prism 4 software from six replicates.(Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 55 mg/mL (82.62 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.5023 mL	7.5113 mL	15.0227 mL
5 mM	0.3005 mL	1.5023 mL	3.0045 mL
10 mM	0.1502 mL	0.7511 mL	1.5023 mL
50 mM	0.030 mL	0.1502 mL	0.3005 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Roberts WG, et al. Cancer Res. 2008, 68(6), 1935-1944.
Serrels A, et al. Int J Cancer. 2012, 131(2), 287-297.
Sun H, et al. Cancer Biol Ther. 2010, 10(1), 38-43.
Bagi CM, et al. Cancer Biol Ther. 2009, 8(9), 856-865.