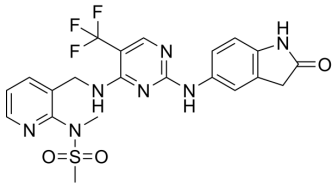
PF-562271

Cat. No.:	HY-10459
CAS No.:	717907-75-0
Molecular Formula:	$C_{21}H_{20}F_3N_7O_3S$
Molecular Weight:	507.49
Target:	FAK; Pyk2
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 66.67 mg/mL (131.37 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9705 mL	9.8524 mL	19.7048 mL
	5 mM	0.3941 mL	1.9705 mL	3.9410 mL
	10 mM	0.1970 mL	0.9852 mL	1.9705 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.67 mg/mL (3.29 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (3.29 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-562271 (VS-6062) is a potent, ATP-competitive and reversible FAK and Pyk2 kinase inhibitor with IC_{50}s of 1.5 nM and 13 nM, respectively[1].

IC_{50} & Target

IC50: 1.5 nM (FAK), 13 nM (Pyk2), 30 nM (CDK2), 47 nM (CDK3), 58 nM (CDK1), 97 nM (CDK7), 97 nM (Flt3)[1]

In Vitro

PF-562271 (VS-6062) is shown to be a 30- to 120-nM inhibitor of CDK2/E, CDK5/p35, CDK1/B, and CDK3/E in recombinant enzyme assays, in cell-based assays evaluating the role of CDKs, a 48-hour exposure of 3.3 μM PF-562271 is required to alter cell cycle progression. PF-562271 is potent in an inducible cell-based assay measuring phospho-FAK with a IC_{50} of 5 nM[1].? ?PF-562271, a selective inhibitor of both FAK and proline-rich tyrosine kinase 2 (PYK2), a FAK-related family member, on cell growth and colony formation in Ewing sarcoma cell lines. Seven cell lines are treated for 5 days with PF-562271 across a

	range of concentrations using 2-fold serial dilutions. Treatment with PF-562271 impaires cell viability in all cell lines, with an average IC_{50} of 2.4 μM after 3 days of treatment. TC32 and A673 are the 2 most sensitive cell lines, with IC_{50} concentrations of 2.1 and 1.7 μM, respectively[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	PF-562271 inhibits FAK phosphorylation in vivo in a dose-dependent fashion (calculated EC_{50} of 93 ng/mL, total) after p.o. administration to tumor-bearing mice[1]. Rats that receive PF-562271 demonstrate a decrease in tumor growth after 2 weeks of treatment with signs of bone healing as evidenced by the deposition of new bone (cortical and cancellous) at sites previously damaged by the tumor[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Ewing sarcoma cells are plated in 10-cm dishes, allowed to adhere for 24 hours, and then treated with PF-562271, PD0325901, or BMS-354825. ATP content is measured as a surrogate for cell number using the CellTiter-Glo Luminescent Cell Viability Assay. Luminescence readings are obtained using the FLUOstar Omega microplate reader. For experiments with small-molecule treatment, 1.25×10^3 Ewing sarcoma cells are seeded in each well and treated with a range of concentrations. IC_{50} values are calculated from ATP measurements obtained after 3 days of treatment using log-transformed, normalized data in GraphPad Prism 5.0. Cell lines are also treated with compound in 6-cm dishes, trypsinized, and counted by light microscopy using trypan blue exclusion. For experiments using shRNA-transduced cells, 1.25×10^3 cells are seeded per well into 384-well plates on day 3 posttransduction. ATP content is measured on days 3, 6, and 8 posttransduction[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1][3]	Mice[1] Athymic female mice (CD-1 Nu/Nu, ~20 grams) are used for all in vivo studies. Exponentially growing cells are trypsinized and resuspended in sterile PBS and inoculated s.c. (1×10^6 cells per mouse in 200 μL) into the right flank of mice. Animals bearing tumors of 150 mm^3 in size are divided into groups receiving either vehicle (5% Gelucire) or PF-562,271 (diluted in vehicle), and dosed by p.o. gavage. Animal body weight and tumor measurements are obtained every 2 d. Tumor volume (mm^3) is measured with Vernier calipers and calculated using the formula: length (mm)×width (mm)×width (mm)×0.5. Percent growth inhibition. For all tumor growth inhibition experiments, 8 to 10 mice per dose group are used. A Student's t test is used to determine the P value. Rats[3] Nude (Crl:NIH-rnu) female rats are used. PF-562271 is formulated for oral dosing using 0.5% methyl-cellulose. On the first day of dosing, rats receive a single dose of PF-562271 (10 mg/kg) by oral gavage. Based on the exposure levels at 1 hour after dosing, the dose is reduced to 5 mg/kg. From the second day onward, rats are dosed daily with 5 mg/kg by oral gavage for 28 days. Dosing is initiated 2 weeks after tumor inoculation and only after the presence of tumors is confirmed by radiography. The presence of the tested compound in serum is confirmed during the course of the study. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Discov. 2022 Sep 6;8(1):84.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Clin Cancer Res. 2019 Jul 15;25(14):4552-4566.
- Cancer Res. 2013 May 1;73(9):2873-83.
- Cell Death Dis. 2023 Feb 24;14(2):157.

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REFERENCES

[1]. Roberts WG, et al. Antitumor activity and pharmacology of a selective focal adhesion kinase inhibitor, PF-562,271. Cancer Res, 2008, 68(6), 1935-1944.

[2]. Crompton BD, et al. High-throughput tyrosine kinase activity profiling identifies FAK as a candidate therapeutic target in Ewing sarcoma. Cancer Res. 2013 May 1;73(9):2873-83.

[3]. Bagi CM, et al. Dual focal adhesion kinase/Pyk2 inhibitor has positive effects on bone tumors: implications for bone metastases. Cancer. 2008 May 15;112(10):2313-21.

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