产品名称：PF-562271
产品别名：PF-562271

生物活性：

Description	PF-562271 is a potent ATP-competitive, reversible inhibitor of FAK and Pyk2 kinase, with an IC_{50} of 1.5 nM and 13 nM, respectively.
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 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 IC50 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 IC50 of 2.4 μM after 3 days of treatment. TC32 and A673 are the 2 most sensitive cell lines, with IC50 concentrations of 2.1 and 1.7 μM, respectively[2].
In Vivo	PF-562271 inhibits FAK phosphorylation in vivo in a dose-dependent fashion (calculated EC50 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].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 48 mg/mL (94.58 mM)** * "≥" means soluble, but saturation unknown.

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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 1.67 mg/mL (3.29 mM); Clear solution

此方案可获得 ≥ 1.67 mg/mL (3.29 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 16.699999 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

	2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 1.67 mg/mL (3.29 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (3.29 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 16.699999 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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. IC50 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].
Animal Administration	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.

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.