产品名称：PP2
产品别名：PP2

生物活性：

Description	PP2 is a reversible and ATP-competitive **Src** family kinases inhibitor with **IC_{50}**s of 4 and 5 nM for **Lck** and **Fyn**, respectively.
IC_{50} & Target	IC50: 4 nM (Lck), 5 nM (Fyn)[1]
In Vitro	At 10 μM, the effect of PP2 on cellular proliferation is not significant, indicating that, at this low concentration, the effect of PP2 on Gemcitabine cytotoxicity does not simply reflect a direct antiproliferative effect, but rather a potentiation of Gemcitabine-induced cytotoxicity. Above 20 μM, growth is increasingly suppressed, a finding consistent with reports in other human cancer cell lines. Although 10 μM PP2 is used in our study, at higher concentrations PP2 is reported to inhibit other intracellular kinases[2]. PP2 is the most widely used commercially available Src family kinase inhibitor. PP2 inhibits Src family kinase activity with IC50 of ~5 nM in vitro, concentrations to 10 μM are often necessary to achieve complete Src family kinase inhibition in cell culture[3].
In Vivo	The tumor growth inhibition rate is 25% in the PP2 treatment group and 5% in the Gemcitabine treatment group (P>0.05). When administered in combination, PP2 and Gemcitabine produce a tumor growth inhibition rate of 98% (P<0.05). Hepatic metastasis occurred in 100% of control and Gemcitabine-treated groups; 88% of the PP2-treated group developed liver metastases. There are no detectable metastases in the group treated with PP2 and Gemcitabine in combination (P<0.05)[2].
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL** (**165.69 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	3.3138 mL	16.5689 mL	33.1378 mL
	5 mM	0.6628 mL	3.3138 mL	6.6276 mL
	10 mM	0.3314 mL	1.6569 mL	3.3138 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 →90% corn oil

Solubility: ≥ 3 mg/mL (9.94 mM); Clear solution

此方案可获得 ≥ 3 mg/mL (9.94 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 30.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。

References	[1]. Hanke JH, et al. Discovery of a novel, potent, and Src family-selective tyrosine kinase inhibitor. Study of Lck-and FynT-dependentT cell activation. J Biol Chem. 1996 Jan 12;271(2):695-701. [2]. Duxbury MS, et al. Inhibition of SRC tyrosine kinase impairs inherent and acquired Gemcitabine resistance in human pancreatic adenocarcinoma cells. Clin Cancer Res. 2004 Apr 1;10(7):2307-18 [3]. Summy JM, et al. AP23846, a novel and highly potent Src family kinase inhibitor, reduces vascular endothelial growth factor and interleukin-8 expression in human solid tumor cell lines and abrogates downstream angiogenic processes. Mol Cancer Ther. 2005 D [4]. Inoue A, et al. Phosphorylation of NMDA receptor GluN2B subunit at Tyr1472 is important for trigeminal processing of itch. Eur J Neurosci. 2016 Oct;44(7):2474-2482.

实验参考：

Cell Assay	Cell growth is determined by MTT assay and confirmed by cell counting. Results of the MTT assay have been shown to correlate well with [^{3}H]thymidine incorporation in pancreatic cancer cell lines. Logarithmically growing cells are plated at 5×10^3 cells/well in 96-well plates, allowed to adhere for 24 h, and cultured in the presence or absence of PP2 and Gemcitabine. Cell proliferation is determined after 96 h. Plates are read using a V_{max} microplate spectrophotometer at a wavelength of 570 nm corrected to 650 nm and normalized to controls. Each independent experiment is performed three times, with 10 determinations for each condition tested. The IC_{50} of Gemcitabine is calculated from these results. At identical time points, cells are trypsinized to form a single cell suspension. Intact cells, determined by trypan blue exclusion, are counted using a Neubauer hemocytometer, and the number of cells per mL is calculated and compared with the control group to confirm the MTT results [2].
Animal Administration	Mice[2] Male athymic nu/nu mice (age, 5 weeks; weight, 20-22 g; specific pathogen free) are anesthetized with i.p. ketamine (200 mg/kg) and xylazine (10 mg/kg) and inoculated with 10^6 Gemcitabine-resistant PANC1^{GemRes} cells in 20 μL of PBS by surgical orthotopic implantation into the pancreas. After inoculation, mice are randomized to three treatment groups: (a) treatment group 1 (n=8) receive 2 mg/kg PP2 in 1% DMSO by i.p. injection three times a week; (b) treatment group 2 (n=8) receive Gemcitabine (100 mg/kg) in the same volume of 1% DMSO vehicle as received by group 1, three times a week; and (c) treatment group 3 (n=8) receive 2 mg/kg PP2 and 100 mg/kg Gemcitabine in the same volume of DMSO as groups 1 and 2, three times a week. The control group receive the same volume of 1% DMSO vehicle as the other groups, three times a week. Treatment is commenced 1 day after implantation, and necropsy is performed 4 weeks after implantation. Primary tumors are identified, weighed, and normalized to total body mass. Tumor growth inhibition rate is calculated using the following formula: tumor growth inhibition rate (%)=$(1-M_T/M_C)\times100$, where M_T and M_C are the mean normalized tumor masses of treatment and control groups, respectively. Liver metastases are counted and confirmed histologically.
References	[1]. Hanke JH, et al. Discovery of a novel, potent, and Src family-selective tyrosine kinase inhibitor. Study of Lck-and FynT-dependentT cell activation. J Biol Chem. 1996 Jan 12;271(2):695-701. [2]. Duxbury MS, et al. Inhibition of SRC tyrosine kinase impairs inherent and acquired Gemcitabine resistance in human pancreatic adenocarcinoma cells. Clin Cancer Res. 2004 Apr 1;10(7):2307-18 [3]. Summy JM, et al. AP23846, a novel and highly potent Src family kinase inhibitor, reduces vascular endothelial growth factor and interleukin-8 expression in human solid tumor cell lines and

	abrogates downstream angiogenic processes. Mol Cancer Ther. 2005 D [4]. Inoue A, et al. Phosphorylation of NMDA receptor GluN2B subunit at Tyr1472 is important for trigeminal processing of itch. Eur J Neurosci. 2016 Oct;44(7):2474-2482.