产品名称：Defactinib
产品别名： VS-6063；PF-04554878

生物活性：

Description	Defactinib (VS-6063; PF-04554878) is a novel FAK inhibitor with potential antiangiogenic and antineoplastic activities.
IC_{50} & Target	FAK[1]
In Vitro	Defactinib (VS-6063) inhibits FAK phosphorylation at the Tyr397 site in a time- and dose-dependent manner. RPPA data shows that Defactinib reduces levels of AKT and YB-1 in taxane-resistant cell lines. The expression of pFAK (Tyr397) is statistically significantly inhibited by Defactinib in a dose-dependent manner in all cell lines. Defactinib inhibits pFAK (Tyr397) expression within 3 hours, with a gradual return of expression by 48 hours[1].
In Vivo	Defactinib (VS-6063) doses of 25 mg/kg twice a day or greater statistically significantly inhibits pFAK (Tyr397) at 3 hours, with return of expression noted by 24 hours. Therefore, administration of Defactinib at 25 mg/kg twice a day is selected as the dosing schedule for subsequent therapy experiments. For therapy experiments, female nude mice bearing HeyA8 tumors in the peritoneal cavity are randomly divided into 4 groups (n=10 per group): 1) vehicle orally twice daily and phosphate-buffered saline intraperitoneally weekly (control); 2) Defactinib 25 mg/kg orally twice daily; 3) PTX intraperitoneally weekly; and 4) both VDefactinib 25 mg/kg orally twice daily and PTX intraperitoneally weekly. There is an 87.4% reduction in tumor weight by PTX monotherapy in the HeyA8 model, and combination therapy resulted in the greatest tumor weight reduction, with a 97.9% reduction (P=0.05 compared with PTX). In the SKOV3ip1 model, a 92.7% tumor weight reduction is observed in the combination group compared with PTX (P<0.001)[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 39 mg/mL (76.40 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	1.9589 mL	9.7945 mL	19.5890 mL
	5 mM	0.3918 mL	1.9589 mL	3.9178 mL
	10 mM	0.1959 mL	0.9795 mL	1.9589 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: ≥ 2.08 mg/mL (4.07 mM); Clear solution

	此方案可获得 ≥ 2.08 mg/mL (4.07 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (4.07 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.07 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Kang Y, et al. Role of focal adhesion kinase in regulating YB-1-mediated resistance in ovarian cancer. J Natl Cancer Inst. 2013 Oct 2;105(19):1485-95.

实验参考：

Animal Administration	Mice[1] To determine the antitumor effects of Defactinib, SKOV3ip1, SKOV3-TR, HeyA8, and HeyA8-MDR cells are injected intraperitoneally. One week after tumor cell injection, mice are randomly assigned to 4 groups of 10 mice (control, PTX alone, Defactinib alone, and PTX with Defactinib); treatment is initiated at 3-4 weeks following injection. PTX at 2 mg/kg (SKOV3ip1 and SKOV3-TR) or 2.5 mg/kg (HeyA8 and HeyA8-MDR) is given intraperitoneally weekly; Defactinib at 25 mg/kg is given orally twice every day. Control mice received HBSS intraperitoneally once a week and vehicle orally twice every day. Mice are monitored daily for adverse effects of therapy and are killed on day 35 (SKOV3ip1 or SKOV3-TR), day 28 (HeyA8 or HeyA8-MDR), or when any of the mice seemed moribund. Total body weight, tumor incidence and mass, and the number of tumor nodules are recorded. Tumors are either fixed in formalin or embedded in paraffin or snap frozen in optimal cutting temperature (OCT) compound in liquid nitrogen.
References	[1]. Kang Y, et al. Role of focal adhesion kinase in regulating YB-1-mediated resistance in ovarian cancer. J Natl Cancer Inst. 2013 Oct 2;105(19):1485-95.