产品名称：Crenolanib (CP-868596)
产品别名：Crenolanib

生物活性：

Description	Crenolanib is a potent and selective inhibitor of wild-type and mutant isoforms of the class III receptor tyrosine kinases FLT3 and PDGFRα/β with K_ds of 0.74 nM and 2.1 nM/3.2 nM, respectively.		
IC_{50} & Target [1]	PDGFRα	PDGFRβ	FLT3
	2.1 nM (Kd)	3.2 nM (Kd)	0.74 nM (Kd)
In Vitro	Crenolanib has 25-fold more affinity for PDGFRA/B compared with KIT, and is approximately 135-fold more potent than STI571 for inhibiting the PDGFRA D842V mutation. The IC50 for crenolanib for a KIT exon 11 deletion mutant kinase is greater than 1,000 versus 8 nM for STI571. Crenolanib has low nanomolar potency against the V561D + D842V-mutant kinase that is similar to its potency against the isolated D842V mutation. Both STI571 and crenolanib potently inhibit the kinase activity of the fusion oncogene with IC50 values of 1 and 21 nM, respectively, and inhibits PDGFRA activation in this cell line with IC50 values of 93 and 26 nM, respectively[1]. HL60/VCR and K562/ABCB1 cells, overexpressing ABCB1, are 6.9- and 3.6-fold resistant to crenolanib, respectively, in relation to parental HL60 and K562 cells. PSC-833 fully reverses resistance to crenolanib in both HL60/VCR and K562/ABCB1 cells. Crenolanib (1 nM-10 μM) stimulates ABCB1 ATPase activity in a concentration-dependent manner. Crenolanib treatment does not increase the cell surface expression of ABCB1. Crenolanib inhibits [^{125}I]-IAAP photocrosslinking of ABCB1 at high concentrations, with 50 % inhibition at 10 μM, but has little effect at lower concentrations, below 1 μM[2]. Crenolanib decreases NSCLC cell viability, induces apoptosis in NSCLC cells, and inhibits cell migration in NSCLC cells[3].		
In Vivo	Crenolanib (10 mg/kg and 20 mg/kg) suppresses non-small-cell lung cancer tumor growth in vivo and induces tumor cell apoptosis, and the dosage of crenolanib applied is well tolerated by recipient mice[3].		

Solvent&Solubility

In Vitro:

DMSO : 33.33 mg/mL (75.15 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2546 mL	11.2729 mL	22.5459 mL
	5 mM	0.4509 mL	2.2546 mL	4.5092 mL
	10 mM	0.2255 mL	1.1273 mL	2.2546 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: ≥ 3 mg/mL (6.76 mM); Clear solution

	此方案可获得 ≥ 3 mg/mL (6.76 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 30.0 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% (20% SBE-β-CD in saline) Solubility: ≥ 3 mg/mL (6.76 mM); Clear solution 此方案可获得 ≥ 3 mg/mL (6.76 mM，饱和度未知) 的澄清溶液。 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 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 3 mg/mL (6.76 mM); Clear solution 此方案可获得 ≥ 3 mg/mL (6.76 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]. Heinrich MC, et al.Crenolanib inhibits the drug-resistant PDGFRA D842V mutation associated with STI571-resistant gastrointestinal stromal tumors. Clin Cancer Res, 2012, Jun 27. [2]. Mathias TJ, et al. The FLT3 and PDGFR inhibitor crenolanib is a substrate of the multidrug resistance protein ABCB1 but does not inhibit transport function at pharmacologically relevant concentrations. Invest New Drugs. 2015 Apr;33(2):300-9. [3]. Wang P, et al. Crenolanib, a PDGFR inhibitor, suppresses lung cancer cell proliferation and inhibits tumor growth in vivo. Onco Targets Ther. 2014 Sep 26;7:1761-8.

实验参考：

Cell Assay	Viable cell numbers following drug treatment are measured using the WST-1 assay. Briefly, 1×10^3 cells are seeded in 100 μL complete medium per well in 96-well tissue culture plates and incubated with crenolanib (0-10 μM) at 37°C in 5% CO_2 for 96 h. 10 μL WST-1 reagent is then added to each well, incubation is continued for two additional hours and the color developed is quantified according to the manufacturer's instructions. Each experiment is performed in triplicate. IC_{50} concentrations are calculated by the least square fit of dose–response inhibition in a non-linear regression model using GraphPad Prism V software. [2]
Animal Administration	A549 cells are injected into the axillary regions of mice (2×10^6 cells/mouse). When the tumor volumes reached 70 mm^3, the mice are randomLy allocated to the control group, low-dose crenolanib group (10 mg/kg), or high-dose crenolanib group (20 mg/kg) (n=6 per group). The vehicle for crenolanib treatment consists of 10% 1-methyl-2-pyrrolidinone and 90% polyethylene glycol 300. The tumor size and mouse body weight are measured every other day for about 2 weeks. The tumor volume is calculated as follows: (mm^3)=(width×width×length)/2. After treatment, the mice are euthanized using carbon dioxide, and the tumors are harvested and analyzed. [3]
References	[1]. Heinrich MC, et al.Crenolanib inhibits the drug-resistant PDGFRA D842V mutation associated with STI571-resistant gastrointestinal stromal tumors. Clin Cancer Res, 2012, Jun 27. [2]. Mathias TJ, et al. The FLT3 and PDGFR inhibitor crenolanib is a substrate of the multidrug resistance protein ABCB1 but does not inhibit transport function at pharmacologically relevant concentrations. Invest New Drugs. 2015 Apr;33(2):300-9.

	[3]. Wang P, et al. Crenolanib, a PDGFR inhibitor, suppresses lung cancer cell proliferation and inhibits tumor growth in vivo. Onco Targets Ther. 2014 Sep 26;7:1761-8.