产品名称：Vatalanib (PTK787) 2HCl
产品别名：瓦他拉尼二盐酸盐；Vatalanib dihydrochloride

生物活性：

Description	Vatalanib dihydrochloride (PTK787 dihydrochloride) is an inhibitor of VEGFR2/KDR with IC50 of 37 nM.
IC_{50} & Target	VEGFR2
	37 nM (IC_{50})
In Vitro	Vatalanib also inhibits Flk, c-Kit and PDGFRβ with IC50 of 270 nM, 730 nM and 580 nM, respectively. Vatalanib shows the anti-proliferation effect by inhibiting thymidine incorporation induced by VEGF in HUVECs with and IC50 of 7.1 nM, and dose-dependently suppresses VEGF-induced survival and migration of endothelial cells in the same dose range without cytotoxic or antiproliferative effect on cells that do not express VEGF receptors[1]. A recent study shows that Vatalanib significantly inhibits the growth of hepatocellular carcinoma cells and enhances the IFN/5-FU induced apoptosis by increasing proteins levels of Bax and reduced Bcl-xL and Bcl-2[2].
In Vivo	Vatalanib induces dose-dependent inhibition of the angiogenic response to VEGF and PDGF in both a growth factor implant model and a tumor cell-driven angiogenesis model after once-daily oral dosing (25-100 mg/kg). In the same dose range, Vatalanib also inhibits the growth and metastasesof several human carcinomas in nude mice without significant effect on circulating blood cells or bone marrow leukocytes[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 125 mg/mL (297.81 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3825 mL	11.9124 mL	23.8248 mL
5 mM	0.4765 mL	2.3825 mL	4.7650 mL
10 mM	0.2382 mL	1.1912 mL	2.3825 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 (4.96 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (4.96 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% (20% SBE-β-CD in saline) Solubility: ≥ 2.08 mg/mL (4.96 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.96 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 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: ≥ 2.08 mg/mL (4.96 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.96 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]. Wood JM, et al. PTK787/ZK 222584, a novel and potent inhibitor of vascular endothelial growth factor receptor tyrosine kinases, impairs vascular endothelial growth factor-induced responses and tumor growth after oral administration. Cancer Res. 2000, 60(8 [2]. Wan J, et al. Local recurrence of small cell lung cancer following radiofrequency ablation is induced by HIF-1α expression in the transition zone. Oncol Rep. 2016 Mar;35(3):1297-308. [3]. Murakami M, et al. Tyrosine kinase inhibitor PTK/ZK enhances the antitumor effects of interferon-α/5-fluorouracil therapy for hepatocellular carcinoma cells. Ann Surg Oncol. 2011, 18(2), 589-596.

实验参考：

Cell Assay	Subconfluent HUVECs are seeded into 96-well plates coated with 1.5% gelatin. After 24 h, growth medium is replaced by basal medium containing 1.5% FCS and a constant concentration of VEGF (50 ng/mL), bFGF (0.5 ng/mL), or FCS (5%), in the presence or absence of Vatalanib. As a control, wells without growth factor are also included. After 24 h of incubation, BrdUrd labeling solution is added, and cells incubated an additional 24 h before fixation, blocking, and addition of peroxidase-labeled anti-BrdUrd antibody. Bound antibody is then detected using 3,3' 5,5'-tetramethylbenzidine substrate[1].
Animal Administration	A porous Teflon chamber (volume, 0.5 mL) is filled with 0.8% w/v agar containing heparin (20 units/mL) with or without growth factor (3 μg/mL human VEGF, 2 μg/mL human PDGF) is implanted s.c. on the dorsal flank of C57/C6 mice. The mice are treated with Vatalanib (12.5, 25 or 50 mg/kg dihydrochloride p.o. once daily) or vehicle (water) starting 1 day before implantation of the chamber and continuing for 5 days after. At the end of treatment, the mice are killed, and the chambers are removed. The vascularized tissue growing around the chamber is carefully removed and weighed, and the blood content is assessed by measuring the hemoglobin content of the tissue[1].
Kinase Assay	Each GST-fused kinase is incubated under optimized buffer conditions. ATP in a total volume of 30 μL in the presence or absence of a test substance (Vatalanib) for 10 min at ambient temperature. The reaction is stopped by adding 10 μL of 250 mM EDTA[1].
References	[1]. Wood JM, et al. PTK787/ZK 222584, a novel and potent inhibitor of vascular endothelial growth factor receptor tyrosine kinases, impairs vascular endothelial growth factor-induced responses and tumor growth after oral administration. Cancer Res. 2000, 60(8 [2]. Wan J, et al. Local recurrence of small cell lung cancer following radiofrequency ablation is induced by HIF-1α expression in the transition zone. Oncol Rep. 2016 Mar;35(3):1297-308.

	[3]. Murakami M, et al. Tyrosine kinase inhibitor PTK/ZK enhances the antitumor effects of interferon-α/5-fluorouracil therapy for hepatocellular carcinoma cells. Ann Surg Oncol. 2011, 18(2), 589-596.