产品名称：SAR131675
产品别名：SAR131675

生物活性：

Description	SAR131675 is a potent and selective VEGFR3 inhibitor with an IC_{50} of 23 nM.
IC_{50} & Target	VEGFR3
	23 nM (IC_{50})
In Vitro	AR131675 is highly selective for VEGFR-3 versus 107 receptors, enzymes, ion channels, and 65 kinases. However, it is moderately active on VEGFR-2 with a VEGFR-3/VEGFR-2 ratio of about 10. SAR131675 inhibits VEGFR-3 tyrosine kinase activity and VEGFR-3 autophosphorylation in HEK cells with IC50 values of 20 and 45 nM, respectively. SAR131675 dose dependently inhibits the proliferation of primary human lymphatic cells, induced by the VEGFR-3 ligands VEGFC and VEGFD, with an IC50 of about 20 nM. SSAR131675 has no antiproliferative activity on a panel of 30 tumors and primary cells, further showing its high specificity and indicating that SAR131675 is not a cytotoxic or cytostatic agent[1].
In Vivo	SAR131675 is very well tolerated in mice and shows a potent antitumoral effect in several orthotopic and syngenic models, including mammary 4T1 carcinoma and RIP1.Tag2 tumors. Interestingly, it significantly reduces lymph node invasion and lung metastasis, showing its antilymphangiogenic activity in vivo. SAR131675 significantly reduces TAM infiltration and aggregation in 4T1 tumors[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 28 mg/mL (78.13 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7903 mL	13.9513 mL	27.9026 mL
	5 mM	0.5581 mL	2.7903 mL	5.5805 mL
	10 mM	0.2790 mL	1.3951 mL	2.7903 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: ≥ 2.25 mg/mL (6.28 mM); Clear solution

此方案可获得 ≥ 2.25 mg/mL (6.28 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 22.5 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: ≥ 2.25 mg/mL (6.28 mM); Clear solution 此方案可获得 ≥ 2.25 mg/mL (6.28 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 22.5 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: ≥ 2.25 mg/mL (6.28 mM); Clear solution 此方案可获得 ≥ 2.25 mg/mL (6.28 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 22.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Alam A, et al. SAR131675, a potent and selective VEGFR-3-TK inhibitor with antilymphangiogenic, antitumoral, and antimetastatic activities. Mol Cancer Ther. 2012 Aug;11(8):1637-49.

实验参考：

Cell Assay	HLMVECs are seeded in 96-well plates coated with 0.3% gelatin (5000 cells per well). Cells are incubated in RPMI 0.1% FCS with VEGFA (10 ng/mL) VEGFC (300 ng/mL), VEGFD (300 ng/mL), or FGF2 (10 ng/mL) in the absence or presence of SAR131675. Five days later, viable cells are quantified with the cell Titer-glo luminescent cell viability assay[1].
Animal Administration	Mouse: Sterile sponge disks impregnated with 200 μg of FGF2 or PBS are subcutaneously introduced on the back of anaesthetized mice. FGF2 is reinjected into the sponges the first 2 days. Daily oral treatment with SAR131675 (30, 100, and 300 mg/kg/d) started the day of sponge implantation. Seven days later, the animals are euthanatized and the sponges are removed, harvested, and lysed in RIPA buffer at 4°C. After a centrifugation at 6,000 × g, the supernatants are collected for further analysis[1].
Kinase Assay	Multiwell plates are precoated with a synthetic polymer substrate poly-Glu-Tyr (polyGT 4:1). The reaction is carried out in the presence of kinase buffer (10×: 50 mM HEPES buffer, pH 7.4, 20 mM $MgCl_2$, 0.1 mM $MnCl_2$, and 0.2 mM Na_3VO_4) supplemented with ATP and dimethyl sulfoxide (DMSO) for the positive control (C+) or SAR131675 (ranging from 3-1,000 nM). ATP is used at 30 μM for VEGFR-1 and VEGFR-3 and at 15 μM for VEGFR-2. The phosphorylated poly-GT is probed with a phosphotyrosine specific monoclonal antibody (mAb) conjugated to horseradish peroxidase and developed in the dark with the HRP chromogenic substrate (OPD). The reaction is then stopped by the addition of 100 μL 1.25 mol/L H_2SO_4, and absorbance is determined using an Envision spectrophotometer at 492 nm [1].
References	[1]. Alam A, et al. SAR131675, a potent and selective VEGFR-3-TK inhibitor with antilymphangiogenic, antitumoral, and antimetastatic activities. Mol Cancer Ther. 2012 Aug;11(8):1637-49.