产品名称：SHP099
产品别名：SHP099

生物活性：

Description	SHP099 is a potent, selective, orally available **SHP2** inhibitor with an **IC_{50}** of 70 nM.
IC_{50} & Target	IC50: 70 nM (SHP2)[1]
In Vitro	The X-ray co-crystal for SHP099 with SHP2 reveals a new interaction with the basic amine and the Phe113 backbone carbonyl. SHP099 shows inhibition of cell proliferation (KYSE-520 model) with an IC50 of 1.4 μM. SHP099 shows high solubility and high permeability with no apparent efflux in Caco-2 cells[1]. SHP099 concurrently binds to the interface of the N-terminal SH2, C-terminal SH2, and protein tyrosine phosphatase domains, thus inhibiting SHP2 activity through an allosteric mechanism. SHP099 suppresses RAS–ERK signalling to inhibit the proliferation of receptor-tyrosine-kinase-driven human cancer cells[2].
In Vivo	After a single doses of 30 and 100 mg/kg (red and blue lines, respectively), dose-dependent exposure and modulation of the pharmacodynamic marker p-ERK is observed in the xenografts. A daily oral dose of 10 or 30 mg/kg yield 19% and 61% tumor growth inhibition, respectively. Tumor stasis is achieved at 100 mg/kg[1].

Solvent&Solubility

In Vitro:

DMSO : 12 mg/mL (34.07 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8388 mL	14.1941 mL	28.3881 mL
	5 mM	0.5678 mL	2.8388 mL	5.6776 mL
	10 mM	0.2839 mL	1.4194 mL	2.8388 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: ≥ 1.2 mg/mL (3.41 mM); Clear solution

此方案可获得 ≥ 1.2 mg/mL (3.41 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 12.0 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: ≥ 1.2 mg/mL (3.41 mM); Clear solution

此方案可获得 ≥ 1.2 mg/mL (3.41 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 12.0 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: ≥ 1.2 mg/mL (3.41 mM); Clear solution 此方案可获得 ≥ 1.2 mg/mL (3.41 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 12.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Garcia Fortanet J, et al. Allosteric Inhibition of SHP2: Identification of a Potent, Selective, and Orally Efficacious Phosphatase Inhibitor. J Med Chem. 2016 Sep 8;59(17):7773-82. [2]. Chen YN, et al. Allosteric inhibition of SHP2 phosphatase inhibits cancers driven by receptor tyrosine kinases. Nature. 2016 Jul 7;535(7610):148-52.

实验参考：

Cell Assay	Cells are plated onto 96-well plates in 100 μL medium. SHP099 with various concentrations (1.25, 2.5, 5, 10, 20 μM) are added 24 h after cell plating. At day 5, 50 μL Celltiter-Glo reagent is added, and the luminescent signal is determined[1].
Kinase Assay	The inhibition of SHP2 from the tested compounds (SHP099) concentrations varying from 0.003-100 μM is monitored using an assay in which 0.5 nM of SHP2 is incubated with of 0.5 μM of peptide IRS1_pY1172(dPEG8)pY1222. After 30-60 minutes incubation at the surrogate substrate, DiFMUP is added to the reaction and incubated at 25 °C for 30 minutes. The reaction is then quenched by the addition of 5 μL of a 160 μM solution of bpV(Phen). The fluorescence signal is monitored using a microplate reader using excitation and emission wavelengths of 340 nm and 450 nm, respectively[1].
References	[1]. Garcia Fortanet J, et al. Allosteric Inhibition of SHP2: Identification of a Potent, Selective, and Orally Efficacious Phosphatase Inhibitor. J Med Chem. 2016 Sep 8;59(17):7773-82. [2]. Chen YN, et al. Allosteric inhibition of SHP2 phosphatase inhibits cancers driven by receptor tyrosine kinases. Nature. 2016 Jul 7;535(7610):148-52.