上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：KPT-9274
产品别名：KPT-9274

生物活性：

Description	KPT-9274 is an orally bioavailable, dual PAK4/Nicotinamide phosphoribosyltransferase (Nampt) inhibitor, with IC_{50}s less than 100 and 120 nM, respectively.	
IC_{50} & Target	PAK4	Nampt
	100 nM (IC_{50})	120 nM (IC_{50})
In Vitro	KPT-9274 attenuates the PAK4/β-catenin pathway, results in NAD depletion, and attenuates viability, invasion, and migration in several RCC cell lines. Inhibition of NAMPT in a cell-free enzymatic assay using recombinant NAMPT shows an IC_{50} of approximately 120 nM for KPT-9274. KPT-9274 attenuates G2–M transit and induces apoptosis in RCC cell lines[2].	
In Vivo	KPT-9274 demonstrates a decrement of xenograft growth comparable with that of sunitinib. There are minimal KPT-9274 effects on the normal human RPTECs and no apparent toxicity in vivo. KPT-9274 is currently being investigated in a phase I human clinical trial of patients with advanced solid malignancies and NHL[2]. KPT-9274 (oral administation; 100mg/kg or 200 mg/kg; twice a day; 14 days) demonstrates a decrement of xenograft growth and exists no significant weight loss in animals receiving KPT-9274. 8 hours after, KPT-9274 are measured at the end of the experiment in mouse plasma and tumors with 10757 ng/ml and 10647 ng/ml, respectively[3].	
	Animal Model:	Mice[1]
	Dosage:	100mg/kg or 200 mg/kg
	Administration:	Oral administation; 100mg/kg or 200 mg/kg; twice a day; 14 days
	Result:	Showed a significant decrease of xenograft growth in KPT-9274 treated mouse.

Solvent&Solubility

In Vitro:

DMSO : 100 mg/mL (**163.77 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6377 mL	8.1883 mL	16.3765 mL
	5 mM	0.3275 mL	1.6377 mL	3.2753 mL
	10 mM	0.1638 mL	0.8188 mL	1.6377 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: ≥ 2.5 mg/mL (4.09 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.09 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 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: 2.5 mg/mL (4.09 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (4.09 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 25.0 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: ≥ 2.5 mg/mL (4.09 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.09 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. WO2015003166A1 [2]. Abu Aboud O, et al. Dual and Specific Inhibition of NAMPT and PAK4 By KPT-9274 Decreases Kidney Cancer Growth. Mol Cancer Ther. 2016 Sep;15(9):2119-29. [3]. Abu Aboud O, et al. Dual and Specific Inhibition of NAMPT and PAK4 By KPT-9274 Decreases Kidney Cancer Growth.Mol Cancer Ther. 2016 Sep;15(9):2119-29.