产品名称：GSK2606414
产品别名：GSK2606414

生物活性：

Description	GSK2606414 is a cell-permeable and orally available **protein kinase R-like endoplasmic reticulum (ER) kinase (PERK)** inhibitor with an **IC_{50}** of 0.4 nM.		
IC_{50} & Target	EIF2AK3 (PERK)	EIF2AK1 (HRI)	EIF2AK2 (PKR)
	0.4 nM (IC_{50})	420 nM (IC_{50})	696 nM (IC_{50})
In Vitro	GSK2606414 inhibits PERK activation in cells[1].		
In Vivo	GSK2606414 (50 and 150 mg/kg, p.o.) inhibits the growth of a human tumor xenograft in mice[1].		

Solvent&Solubility

In Vitro:

DMSO : ≥ 31 mg/mL (68.67 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2151 mL	11.0757 mL	22.1513 mL
	5 mM	0.4430 mL	2.2151 mL	4.4303 mL
	10 mM	0.2215 mL	1.1076 mL	2.2151 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 (5.54 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.54 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 (5.54 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (5.54 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 (5.54 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.54 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]. Axten JM, et al. Discovery of 7-methyl-5-(1-{[3-(trifluoromethyl)phenyl]acetyl}-2,3-dihydro-1H-indol-5-yl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine (GSK2606414), a potent and selective first-in-class inhibitor of protein kinase R (PKR)-like endoplasmic reticulu [2]. Zhang M, et al. Inhibiting the Plasmodium eIF2α Kinase PK4 Prevents Artemisinin-Induced Latency. Cell Host Microbe. 2017 Dec 13;22(6):766-776.e4.

实验参考：

Animal Administration	Exponentially growing BxPC3 tumor cells (10×10^6 cells/mouse) from cell culture are implanted subcutaneously into the right flank of female nude mice. Sixteen days after implantation, mice with ~200 mm^3 tumors are randomized into various treatment groups (n=8 mice/group). Animals are orally treated with vehicle (0.5% hydoxypropylmethylcellulose, 0.1% Tween 80 in water, pH 4.8), compound at 50 or 150 mg/kg, b.i.d. for 21 days. Tumor volume is measured twice weekly with calipers and calculated. Results are represented as percent inhibition on completion of dosing, which is 100[1-(average growth of drug-treated population)/(average growth of vehicle-treated control population)]. Statistical analysis is performed using a two-tailed t test. [1]
References	[1]. Axten JM, et al. Discovery of 7-methyl-5-(1-{[3-(trifluoromethyl)phenyl]acetyl}-2,3-dihydro-1H-indol-5-yl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine (GSK2606414), a potent and selective first-in-class inhibitor of protein kinase R (PKR)-like endoplasmic reticulu [2]. Zhang M, et al. Inhibiting the Plasmodium eIF2α Kinase PK4 Prevents Artemisinin-Induced Latency. Cell Host Microbe. 2017 Dec 13;22(6):766-776.e4.