产品名称：GSK2334470
产品别名：GSK2334470

生物活性：

Description	GSK2334470 is a highly specific and potent inhibitor of **PDK1** with an **IC_{50}** of 10 nM.
IC_{50} & Target	IC50: 10 nM(PDK1)[1]
In Vitro	Small molecule GSK2334470 inhibits PDK1 with an IC50 of ~10 nM, but does not suppress the activity of 93 other protein kinases including 13 AGC-kinases most related to PDK1 at 500-fold higher concentrations. Addition of GSK2334470 ablates T-loop residue phosphorylation and activation of SGK isoforms and S6K1 induced by serum or IGF-1 (insulin-like growth factor 1). GSK2334470 and AZD8055 effectively inhibite phosphorylation of PDK1 and mTOR, respectively, and induce higher G0–G1 ratio in LAN-1-MK than that in LAN-1 as well. PDK1 and mTOR inhibitors effecte on phosphorylation of GSK3β in some of resistant sublines[2].
In Vivo	The efficacy of the PDK1 inhibitor (PDKi) GSK2334470 is tested in newborn BrafV600E::Pten−/−mice subjected to systemic administration of 4-HT. Twice weekly administration of PDK1 results in marked inhibition of pigmented lesions and concomitant melanomagenesis, as well as significant inhibition of lung metastases, seen by H&E staining-based quantification (~80%), and lymph node metastases as by S100 immunostaining, similar to the phenotype seen upon genetic ablation of Pdk1[3].

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (108.09 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1617 mL	10.8087 mL	21.6174 mL
	5 mM	0.4323 mL	2.1617 mL	4.3235 mL
	10 mM	0.2162 mL	1.0809 mL	2.1617 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 (5.40 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.40 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 (5.40 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.40 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 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 (5.40 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.40 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]. Najafov A, et al. Characterization of GSK2334470, a novel and highly specific inhibitor of PDK1. Biochem J.?2011 Jan 15;433(2):357-69. [2]. Qi L, et al. PDK1-mTOR signaling pathway inhibitors reduce cell proliferation in MK2206 resistant neuroblastoma cells. Cancer Cell Int.?2015 Sep 29;15:91. [3]. Scortegagna M, et al. Genetic inactivation or pharmacological inhibition of Pdk1 delays development and inhibits metastasis of Braf(V600E)::Pten(-/-) melanoma. Oncogene. 2014 Aug 21;33(34):4330-9.

实验参考：

Cell Assay	GSK2334470 is dissolved in DMSO and diluted with appropriate medium before use. To study the inhibitory effect of GSK2334470 on mTOR-S6K pathway, non-resistant cells and the resistant sublines are treated with GSK2334470 at 5 μM for 1.5 and 12 h in 10 % FBS medium with/without MK-2206 (5 μM)[2].
Animal Administration	Mice is dissolved in DMSO and then diluted with PBS or saline. BrafV600E::Pten−/− are generated as previously described. Cohorts of six animals per group are used in each experimental group. GSK2334470 is administered through IP injection (100 mg/kg) 3 times per week starting the same day of topical administration of 4-hydroxytamoxifen and ending at the time of mouse collection, based on earlier studies[3].
References	[1]. Najafov A, et al. Characterization of GSK2334470, a novel and highly specific inhibitor of PDK1. Biochem J.?2011 Jan 15;433(2):357-69. [2]. Qi L, et al. PDK1-mTOR signaling pathway inhibitors reduce cell proliferation in MK2206 resistant neuroblastoma cells. Cancer Cell Int.?2015 Sep 29;15:91. [3]. Scortegagna M, et al. Genetic inactivation or pharmacological inhibition of Pdk1 delays development and inhibits metastasis of Braf(V600E)::Pten(-/-) melanoma. Oncogene. 2014 Aug 21;33(34):4330-9.