产品名称：**GSK923295**
产品别名：**GSK-923295**

生物活性：

Description	GSK-923295 is a special, allosteric inhibitor of centromere-associated protein-E (CENP-E) kinesin motor ATPase activity, with Ki of 3.2±0.2 nM and 1.6± 0.1 nM for human and canine, respectively.
IC_{50} & Target	CENP-E
	1.6 nM (Ki, Canine CENP
In Vitro	GSK-923295 (GSK923295) is a first-in-class, specific, allosteric inhibitor of CENP-E kinesin motor function. GSK923295 is uncompetitive with both ATP and MT, inhibiting CENP-E MT-stimulated ATPase activity with a Ki of 3.2±0.2 nM and 1.6±0.1 nM for human and canine, respectively. GSK923295 inhibits release of inorganic phosphate and stabilized CENP-E motor domain interaction with microtubules[1]. GSK923295 has broad growth inhibitory activity in a panel of 237 cancer cell lines and produces significant tumor growth-delay in 8 of the 11 mouse xenograft tumor models with IC_{50}s of 17.2 nM, 55.6 nM, 42 nM, and 51.9 nM for SW48, RKO (BRAF mutant), SW620 (KRAS mutant), and HCT116 (KRAS mutant), respectively[2]. GSK923295 is a potent and selective small molecule inhibitor of human CENPE with a Ki of 3.2 nM. GSK923295 demonstrates broad efficacy against a panel of 19 human neuroblastoma derived cell lines with an average growth IC_{50} of 41 nM[3].
In Vivo	Xenografts of mice treated with GSK-923295 (GSK923295) shows significant tumor growth delay compared to the control arm (NB-EBc1 p<0.0001; NB-1643 p=0.018; NB-1691 p=0.0018)[3].
Solvent&Solubility	***In Vitro:***
	DMSO : 30 mg/mL (**50.66 mM;** Need ultrasonic)
	H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6888 mL	8.4441 mL	16.8882 mL
	5 mM	0.3378 mL	1.6888 mL	3.3776 mL
	10 mM	0.1689 mL	0.8444 mL	1.6888 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: ≥ 3 mg/mL (5.07 mM); Clear solution

此方案可获得 ≥ 3 mg/mL (5.07 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 30.0 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: 3 mg/mL (5.07 mM); Suspended solution; Need ultrasonic 此方案可获得 3 mg/mL (5.07 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 30.0 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: ≥ 3 mg/mL (5.07 mM); Clear solution 此方案可获得 ≥ 3 mg/mL (5.07 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 30.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Wood KW, et al. Antitumor activity of an allosteric inhibitor of centromere-associated protein-E. Proc Natl Acad Sci U S A. 2010 Mar 30;107(13):5839-44. [2]. Mayes PA, et al. Mitogen-activated protein kinase (MEK/ERK) inhibition sensitizes cancer cells to centromere-associated protein E (CENP-E) inhibition. Int J Cancer. 2013 Feb 1;132(3):E149-57. [3]. Balamuth NJ, et al. Serial transcriptome analysis and cross-species integration identifies centromere-associated protein E as a novel neuroblastoma target. Cancer Res. 2010 Apr 1;70(7):2749-58.

实验参考：

Cell Assay	Cell-growth inhibition assays are performed by MDS in 384-well plates, and DNA content of fixed cells stained with DAPI using an Incell 1000 (GE) is analyzed. DNA content is determined 24 h after seeding (T_0) and after exposure to varying concentrations of GSK-923295 (0.01 nM, 0.1 nM, 1 nM, 10 nM, 100 nM, 1 μM, 10 μM, and 100 μM) for an additional 72 h (T_{72}). All T_{72} measurements are normalized to T_0. Curves are analyzed using the XLfit curve-fitting tool to determine the concentration of GSK923295 yielding 50% growth inhibition relative to T_0 and Y_{max} values (GI_{50}) [1]
Animal Administration	Mice[3] CB17 *scid* mice are used to propagate subcutaneously implanted neuroblastoma tumors. Tumor diameters are measured using calipers. Tumor volumes are calculated. Once tumor volume exceeds 200 mm^3, mice are randomized (n=10 per arm) to receive either GSK923295 125 mg/kg IP or vehicle (96% acidified water, 2% DMAC, 2% CREM) for a total of 6 doses using a 3 days on, 4 days off, 3 days on regimen.
References	[1]. Wood KW, et al. Antitumor activity of an allosteric inhibitor of centromere-associated protein-E. Proc Natl Acad Sci U S A. 2010 Mar 30;107(13):5839-44. [2]. Mayes PA, et al. Mitogen-activated protein kinase (MEK/ERK) inhibition sensitizes cancer cells to centromere-associated protein E (CENP-E) inhibition. Int J Cancer. 2013 Feb 1;132(3):E149-57. [3]. Balamuth NJ, et al. Serial transcriptome analysis and cross-species integration identifies centromere-associated protein E as a novel neuroblastoma target. Cancer Res. 2010 Apr 1;70(7):2749-58.