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：LY2606368
产品别名：Prexasertib

生物活性：

Description	Prexasertib (LY2606368) is a potent, selective and ATP-competitive checkpoint kinase 1 (Chk1) inhibitor, with an IC50 and a Ki of <1 nM and 0.9 nM, respectively.		
IC_{50} & Target	Chk1	Chk1	Chk2
	0.9 nM (Ki)	<1 nM (IC_{50})	8 nM (IC_{50})
In Vitro	Prexasertib (LY2606368) is a potent and selective ATP competitive inhibitor of Chk1, with an IC50 of <1 nM, and also inhibits CHK2, with an IC50 of 8 nM. Prexasertib has an EC50 of 1 nM for CHK1 activity through autophosphorylation of serine 296 and <31 nM for HT-29 CHK2 autophosphorylation (S516). Prexasertib potently abrogates the G2-M checkpoint activated by NSC 123127 in p53-deficient HeLa cells with an EC50 of 9 nM. However, 100 nM Prexasertib does not inhibit PMA-stimulated RSK but instead weakly stimulates phosphorylation of S6 on serines 235/236. Prexasertib is broadly antiproliferative with IC50s of 3 nM, 3 nM, 10 nM, 37 nM, and 68 nM against U-2 OS, Calu-6, HT-29, HeLa, and NCI-H460 cell lines, respectively. Prexasertib (4 nM) results in a large shift in cell-cycle populations from G1 and G2-M to S-phase with an accompanied induction of H2AX phosphorylation in U-2 OS cells[1]. Prexasertib (LY2606368; 25 μM) exhibits inhibitory activities against proliferation of AGS and MKN1 cells. Prexasertib (20 nM) inhibits HR repair capacity DR-GFP cells. Prexasertib (5 nM) in combination with PARP inhibitor BMN673, displays synergistic anticancer effects in gastric cancer cells[2].		
In Vivo	Prexasertib (LY2606368; 15 mg/kg, s.c.) significantly inhibits tumor growth in xenograft tumor models with less animal weight loss[1]. Prexasertib (LY2606368; 2 mg/kg, s.c.) and BMN673 combination has synergistic anticancer effect in gastric cancer PDX model, and the effect is higher than that of one drug alone[2].		

Solvent&Solubility

In Vitro:

DMSO： 16.67 mg/mL (45.62 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7368 mL	13.6840 mL	27.3680 mL
5 mM	0.5474 mL	2.7368 mL	5.4736 mL
10 mM	0.2737 mL	1.3684 mL	2.7368 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

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	1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 1.67 mg/mL (4.57 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (4.57 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 16.699999 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。
References	[1]. King C, et al. LY2606368 Causes Replication Catastrophe and Antitumor Effects through CHK1-Dependent Mechanisms. Mol Cancer Ther. 2015 Sep;14(9):2004-1 [2]. Yin Y, et al. Chk1 inhibition potentiates the therapeutic efficacy of PARP inhibitor BMN673 in gastric cancer. Am J Cancer Res. 2017 Mar 1;7(3):473-483.

实验参考：

Cell Assay	Proliferation inhibition effect of Chk1 ablation, IR sensitivity, anticancer effect of BMN673 and Prexasertib are detected by MTS Cell Proliferation Colorimetric Assay Kit. Cells are seeded into 96 wells cell culture plate, then treated with indicated experiment conditions, then added 20 μL MTS reagent to each well subsequently, after incubated for 2 hours, cell viability of each well is detected on microplate reader at a wavelength of 490 nM[2].
Animal Administration	Female CD-1 nu-/nu- mice (26-28 g) are used for this study. Tumor growth is initiated by subcutaneous injection of 1×10^6 Calu-6 cells in a 1:1 mixture of serum-free growth medium and Matrigel in the rear flank of each subject animal. When tumor volumes reach approximately 150 mm^3 in size, the animals are randomized by tumor size and body weight, and placed into their respective treatment groups. Vehicle consisting of 20% Captisol pH4 or Prexasertib is administered by subcutaneous injection in a volume of 200 μL. Four, eight, 12, 24, and 48 hours after drug administration, blood for plasma drug exposure is extracted via cardiac puncture and assayed on a Sciex API 4000 LC/MS-MS system. The xenograft tissue is promptly removed and prepared. Lysates are analyzed by immunoblot analysis for protein phosphorylation levels. Group means, SEs and P values are calculated using Kronos. [1]
References	[1]. King C, et al. LY2606368 Causes Replication Catastrophe and Antitumor Effects through CHK1-Dependent Mechanisms. Mol Cancer Ther. 2015 Sep;14(9):2004-1 [2]. Yin Y, et al. Chk1 inhibition potentiates the therapeutic efficacy of PARP inhibitor BMN673 in gastric cancer. Am J Cancer Res. 2017 Mar 1;7(3):473-483.