产品名称：2-Pyrimidinamine, N-[5-[(4-ethyl-1-piperazinyl)methyl]-2-pyridinyl]-5-fluoro-4-[4-fluoro-2-methyl-1-(1-methylethyl)-1H-benzimida

产品别名：Abemaciclib methanesulfonate

生物活性：

Description	Abemaciclib methanesulfonate (LY2835219 methanesulfonate) is a selective **CDK4/6** inhibitor with **IC_{50}**s of 2 nM and 10 nM for CDK4 and CDK6, respectively.

IC_{50} & Target

Cdk4/cyclin D1	CDK6/cyclinD1	CDK9/cyclinT1	CDK5/p35	Cdk5/p25
2 nM (IC_{50})	10 nM (IC_{50})	57 nM (IC_{50})	287 nM (IC_{50})	355 nM (IC_{50})
CDK2/cyclinE	CDK1/cyclinB1	CDK7/Mat1/cyclinH1	PIM1	PIM2
504 nM (IC_{50})	1627 nM (IC_{50})	3910 nM (IC_{50})	50 nM (IC_{50})	3400 nM (IC_{50})
HIPK2	DYRK2	CK2	GSK3b	JNK3
31 nM (IC_{50})	61 nM (IC_{50})	117 nM (IC_{50})	192 nM (IC_{50})	389 nM (IC_{50})
FLT3 (D835Y)	DRAK1	FLT3		
403 nM (IC_{50})	659 nM (IC_{50})	3960 nM (IC_{50})		

In Vitro	Abemaciclib (LY2835219) reduces cell viability with the IC50 values ranging from 0.5 μM to 0.7 μM, inhibits Akt and ERK signaling but not mTOR activation at head and neck squamous cell carcinoma (HNSCC) cells[1]. Abemaciclib (LY2835219) shows inhibition on A375R1-4, M14R, and SH4R with EC50 values ranging from 0.3 to 0.6 μM; Abemaciclib inhibits the proliferation of the parental A375 and resistant A375RV1 and A375RV2 cells with similar potencies with IC50 values of 395, 260, and 463 nM, respectively[2]. Abemaciclib (LY2835219) inhibits CDK4 and CDK6 with low nanomolar potency, inhibits Rb phosphorylation resulting in a G1 arrest and inhibition of proliferation, and its activity is specific for Rb-proficient cells[3].
In Vivo	Abemaciclib (LY2835219) (45 mg/kg, p.o.) in combination with RAD001 causes a cooperative antitumor effect in HNSCC xenograft tumor[1]. Abemaciclib (LY2835219) (45 or 90 mg/kg, p.o.) shows significant tumor growth inhibition in an A375 xenograft model[2].

In Vitro:

H_2O : 125 mg/mL (207.40 mM; Need ultrasonic)

DMSO : ≥ 25 mg/mL (41.48 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.6592 mL	8.2960 mL	16.5920 mL
5 mM	0.3318 mL	1.6592 mL	3.3184 mL
10 mM	0.1659 mL	0.8296 mL	1.6592 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:

Solvent&Solubility	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: ≥ 2.08 mg/mL (3.45 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (3.45 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (3.45 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (3.45 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (3.45 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (3.45 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Ku BM, et al. The CDK4/6 inhibitor LY2835219 has potent activity in combination with mTOR inhibitor in head and neck squamous cell carcinoma. Oncotarget. 2016 Mar 22;7(12):14803-13. [2]. Yadav V, et al. The CDK4/6 inhibitor LY2835219 overcomes PLX4032 resistance resulting from MAPK reactivation and cyclin D1 upregulation. Mol Cancer Ther. 2014 Oct;13(10):2253-63. [3]. Gelbert LM, et al. Preclinical characterization of the CDK4/6 inhibitor LY2835219: in-vivo cell cycle-dependent/independent anti-tumor activities alone/in combination with NSC 613327. Invest New Drugs. 2014 Oct;32(5):825-37. [4]. Wu T, et al. Effect of abemaciclib (LY2835219) on enhancement of chemotherapeutic agents in ABCB1 and ABCG2 overexpressing cells in vitro and in vivo. Biochem Pharmacol. 2017 Jan 15;124:29-42.

实验参考：

Cell Assay	Cells are seeded in a 96-well plate, allowed to adhere overnight, and treated with DMSO control (0.1% v/v) or the indicated compounds for 72 h. Cell viability and proliferation are determined using a Cell Counting Kit according to the manufacturer's instructions. The interaction between Abemaciclib (LY2835219) and mTOR inhibitor is determined using CompuSyn. Combination index (CI) values of 1 indicates and additive drug interaction, whereas a CI of < 1 is synergistic and a CI of > 1 is antagonistic. [1]
	Six-week-old BALB/c female nude mice are injected subcutaneously with OSC-19 (1×10^6) cells. When tumor sizes reach approximately 100 mm^3, mice are randomized by tumor size and subjected to each treatment. At least 5 mice per treatment group are included. Each group of mice is dosed via daily oral gavage with vehicle, Abemaciclib (LY2835219) (45 mg/kg/d or 90 mg/kg/d), RAD001 (5

Animal Administration	mg/kg/d), or a combination of both. The Abemaciclib (LY2835219) is dissolved in 1% HEC in 20 mM phosphate buffer (pH2.0). Tumor size and body weight are measured twice weekly. Tumor volumes are calculated using the following formula: $V=(L \times W^2)/2$ (L, Length; W, width). Mice are gavaged a final time on day 14 and sacrificed the following day. The tumors are removed for Western blot and immunohistochemistry. [1]
References	[1]. Ku BM, et al. The CDK4/6 inhibitor LY2835219 has potent activity in combination with mTOR inhibitor in head and neck squamous cell carcinoma. Oncotarget. 2016 Mar 22;7(12):14803-13. [2]. Yadav V, et al. The CDK4/6 inhibitor LY2835219 overcomes PLX4032 resistance resulting from MAPK reactivation and cyclin D1 upregulation. Mol Cancer Ther. 2014 Oct;13(10):2253-63. [3]. Gelbert LM, et al. Preclinical characterization of the CDK4/6 inhibitor LY2835219: in-vivo cell cycle-dependent/independent anti-tumor activities alone/in combination with NSC 613327. Invest New Drugs. 2014 Oct;32(5):825-37. [4]. Wu T, et al. Effect of abemaciclib (LY2835219) on enhancement of chemotherapeutic agents in ABCB1 and ABCG2 overexpressing cells in vitro and in vivo. Biochem Pharmacol. 2017 Jan 15;124:29-42.