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产品名称：LY3214996
产品别名：LY3214996

生物活性：

Description	LY3214996 is a highly selective inhibitor of ERK1 and ERK2, with IC50 of 5 nM for both enzymes in biochemical assays. LY3214996 potently inhibits cellular p-RSK1 in BRAF and RAS mutant cancer cell lines. LY3214996 shows potent antitumor activities in cancer models with MAPK pathway alterations.	
IC_{50} & Target	ERK1	ERK2
	5 nM (IC_{50})	5 nM (IC_{50})
In Vitro	LY3214996 is a highly selective inhibitor of ERK1 and ERK2, with IC_{50} of 5 nM for both enzymes in biochemical assays. LY3214996 potently inhibits cellular phospho-RSK1 in BRAF and RAS mutant cancer cell lines. In an unbiased tumor cell panel sensitivity profiling for inhibition of cell proliferation, tumor cells with MAPK pathway alterations including BRAF, NRAS or KRAS mutation are generally sensitivity to LY3214996[1].	
In Vivo	In tumor xenograft models, LY3214996 inhibits PD biomarker phospho-p90RSK1 in tumors and the PD effects are correlated with compound exposures and anti-tumor activities. LY3214996 shows either similar or superior anti-tumor activity as compared to other published ERK inhibitors in BRAF or RAS mutant cell lines and xenograft models. Oral administration of single-agent LY3214996 significantly inhibits tumor growth in vivo and is well tolerated in BRAF or NRAS mutant melanoma, BRAF or KRAS mutant colorectal, lung and pancreatic cancer xenografts or PDX models. Therefore, LY3214996 can be tailored for treatment of cancers with MAPK pathway alteration. In addition, LY3214996 has anti-tumor activity in a Vemurafenib-resistant A375 melanoma xenograft model due to MAPK reactivation, may have potential for treatment of melanoma patients who have failed BRAF therapies. More importantly, LY3214996 can be combined with investigational and approved agents in preclinical models, particularly KRAS mutant models. Combination treatment of LY3214996 and CDK4/6 inhibitor abemaciclib is well tolerated and results in potent tumor growth inhibition or regression in multiple in vivo cancer models, including KRAS mutant colorectal and non-small cell lung cancers[1].	

In Vitro:

DMSO : 20 mg/mL (44.10 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	2.2048 mL	11.0239 mL	22.0478 mL
	5 mM	0.4410 mL	2.2048 mL	4.4096 mL
	10 mM	0.2205 mL	1.1024 mL	2.2048 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：

Solvent&Solubility	——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 mg/mL (4.41 mM); Clear solution 此方案可获得 ≥ 2 mg/mL (4.41 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.0 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 mg/mL (4.41 mM); Clear solution 此方案可获得 ≥ 2 mg/mL (4.41 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.0 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 mg/mL (4.41 mM); Clear solution 此方案可获得 ≥ 2 mg/mL (4.41 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 20.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Shripad V. Bhagwat, et al. Abstract 4973: Discovery of LY3214996, a selective and novel ERK1/2 inhibitor with potent antitumor activities in cancer models with MAPK pathway alterations. Cancer Research. July 2017.