产品名称：**BYL719**
产品别名：**Alpelisib**

生物活性：					
Description	Alpelisib (BYL-719) is a potent, selective, and orally active PI3Kα inhibitor. Alpelisib (BYL-719) shows efficacy in targeting PIK3CA-mutated cancer. Alpelisib (BYL-719) also inhibits p110α/γ/δ/β with IC50s of 5/250/290/1200 nM, respectively. Antineoplastic activity[1][2][3].				
IC_{50} & Target	p110α	p110γ	p110δ	p110β	p110α-H1047R
	5 nM (IC_{50})	250 nM (IC_{50})	290 nM (IC_{50})	1200 nM (IC_{50})	4 nM (IC_{50})
	p110α-E545K				
	4 nM (IC_{50})				
In Vitro	AAlpelisib (BYL-719) potently inhibits the 2 most common PIK3CA somatic mutations (H1047R, E545K; IC50s~4 nM). Alpelisib potently inhibits Akt phosphorylation in cells transformed with PI3Kα (IC50=74±15 nM) and shows significant reduced inhibitory activity in PI3K β or PI3K δ isoforms transformed cells (≥ 15-fold compared with PI3K α)[2]. Alpelisib (BYL-719, 0-50 μM; 72 hours) inhibits the cell growth of osteosarcoma cell lines MG63, HOS, POS-1 and MOS-J in a dose-dependent manner[3]. Alpelisib (BYL-719) significantly alters the distribution of cell cycle phases. Alpelisib (BYL-719, 25 μM; 18 hours) induces a cell cycle arrest in the G0/G1 phase of human and murine osteosarcoma cell lines[3].				
	Cell Proliferation Assay[3]				
	Cell Line:	MG63, HOS, POS-1, MOS-J			
	Concentration:	10, 20, 30, 40, 50 μM			
	Incubation Time:	72 hours			
	Result:	Inhibited the cell growth of all osteosarcoma cell lines tested in a dose-dependent manner with IC_{50}s of 6-15 μM and with IC_{90}s of 24-42 μM.			
	Cell Cycle Analysis[3]				
	Cell Line:	MG63, HOS, POS-1, MOS-J			
	Concentration:	25 μM			
	Incubation Time:	18 hours			
	Result:	Induced a cell cycle arrest in the G0/G1 phase of human and murine osteosarcoma cell .			
In Vivo	Alpelisib (BYL-719) (12.5 mg/kg and 50 mg/kg for C57Bl/6J mice; 50 mg/kg for female Rj:NMRI-nude mice; oral administration; daily) significantly reduces tumor volumes and deposition of ectopic bone matrix[3]. Alpelisib has moderate terminal elimination half-life (t1/2=2.9±0.2 h) for rat (1 mg/kg, iv) [1].				
	Animal Model:	A 5-week-old female Rj:NMRI-nude mice with human HOS-MNNG osteosarcoma cells; A 5-week-old male C57Bl/6J mice with mouse MOS-J osteosarcoma cells[3]			
	Dosage:	12.5 mg/kg and 50 mg/kg for C57Bl/6J mice; 50 mg/kg for female Rj:NMRI-nude mice			
	Administration:	Oral administration; daily			
	Result:	Significantly reduced tumor volumes and simultaneously reduced tumor growth.			
	Animal Model:	Female Sprague Dawley rats [1]			
	Dosage:	1 mg/kg (Pharmacokinetic Study)			

	Administration:	I.V.
	Result:	t1/2=2.9±0.2 hours.

Solvent&Solubility

In Vitro:

DMSO： ≥ 100 mg/mL (226.52 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2652 mL	11.3258 mL	22.6516 mL
	5 mM	0.4530 mL	2.2652 mL	4.5303 mL
	10 mM	0.2265 mL	1.1326 mL	2.2652 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 (5.66 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.66 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 (5.66 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.66 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 (5.66 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.66 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]. Furet P, et al. Discovery of NVP-BYL719 a potent and selective phosphatidylinositol-3 kinase alpha inhibitor selected for clinical evaluation. Bioorg Med Chem Lett. 2013 Jul 1;23(13):3741-8.

[2]. Fritsch C, et al. Characterization of the novel and specific PI3Kα inhibitor NVP-BYL719 and development of the patient stratification strategy for clinical trials. Mol Cancer Ther. 2014 May;13(5):1117-29.

	[3]. Gobin B, et al. BYL719, a new α-specific PI3K inhibitor: single administration and in combination with conventional chemotherapy for the treatment of osteosarcoma. Int J Cancer. 2015 Feb 15;136(4):784-96.