产品名称：INK 128 (MLN0128)
产品别名：Sapanisertib；沙帕色替

生物活性：

Description

Sapanisertib (INK-128; MLN0128; TAK-228) is an orally available, ATP-dependent **mTOR1/2** inhibitor with an **IC_{50}** of 1 nM for mTOR kinase.

IC_{50} & Target

mTOR	mTORC1	mTORC2	PI3Kα	PI3Kγ	PI3Kδ
1 nM (IC_{50})			219 nM (IC_{50})	221 nM (IC_{50})	230 nM (IC_{50})
PI3Kβ	Autophagy				
5.293 μM (IC_{50}					

In Vitro

Sapanisertib (INK-128) exhibits an enzymatic inhibition activity against mTOR and more than 100-fold selectivity to PI3K kinases[1]. Sapanisertib (INK-128) selectively decreases the expression of YB1, MTA1, vimentin and CD44 at the protein but not transcript level in PC3 cells. Sapanisertib (INK-128) decreases the invasive potential of PC3 prostate cancer cells. Furthermore, Sapanisertib (INK-128) inhibits cancer cell migration starting at 6 h of treatment, precisely correlating with when decreases in the expression of pro-invasion genes are evident, but preceding any changes in the cell cycle or overall global protein synthesis[2].

In Vivo

In a ZR-75-1 breast cancer xenograft model, Sapanisertib (INK-128) shows tumor growth inhibition efficacy at a dose of 0.3 mg/kg/day[1]. 4EBP1 and p70S6K1/2 phosphorylation is completely restored to wild-type levels after treatment with INK128 in PtenL/L mice. Sapanisertib (INK-128) treatment results in a 50% decrease in prostatic intraepithelial neoplasia (PIN) lesions in PtenL/L mice and induces programmed cell death in multiple cancer cell lines in mice[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 83.3 mg/mL (269.29 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.2328 mL	16.1640 mL	32.3279 mL
	5 mM	0.6466 mL	3.2328 mL	6.4656 mL
	10 mM	0.3233 mL	1.6164 mL	3.2328 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 (8.08 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (8.08 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 (8.08 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.08 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。
References	[1]. Liu A, et al. mTOR Mediated Anti-Cancer Drug Discovery. Drug Discovery Today: Therapeutic Strategies. 2009, 6(2), 47-55. [2]. Hsieh AC, et al. The translational landscape of mTOR signalling steers cancer initiation and metastasis. Nature. 2012 Feb 22;485(7396):55-61.

实验参考：

Cell Assay	PC3 cells are treated with the appropriate drug for 48 h, and proliferation is measured using CellTiter-Glo Luminescent reagent. The concentration of Sapanisertib (INK-128) necessary to achieve inhibition of cell growth by 50% (IC_{50}) is calculated using concentrations ranging from 20.0 μM to 0.1 nM (12-point curve). [2]
Animal Administration	Nude mice are inoculated subcutaneously in the right subscapular region with 5×10^6 MDA-MB-361 cells. After tumours reach a size of 150-200 mm^3, mice are randomLy assigned into vehicle control or treatment groups. Sapanisertib (INK-128) is formulated in 5% polyvinylpropyline, 15% NMP, 80% water and administered by oral gavage at 0.3 mg/kg and 1 mg/kg daily. [2]
References	[1]. Liu A, et al. mTOR Mediated Anti-Cancer Drug Discovery. Drug Discovery Today: Therapeutic Strategies. 2009, 6(2), 47-55. [2]. Hsieh AC, et al. The translational landscape of mTOR signalling steers cancer initiation and metastasis. Nature. 2012 Feb 22;485(7396):55-61.