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产品名称：ISA-2011B
产品别名：ISA-2011B

生物活性：

Description	ISA-2011B is a PIP5Kα inhibitor with promising anticancer effects .
In Vitro	The proliferation rate of PC-3 cells after treatment with ISA-2011B at 10, 20, and 50 μM is significantly reduced to 58.77%, 48.65%, and 21.62% of vehicle-treated controls, respectively. ISA-2011B exhibits the highest binding affinity to PIP5K1α, and to MAP/microtubule affinity-regulating kinase 1 and 4 (MARK1 and MARK4) across 460 kinases. ISA-2011B treatment inhibits PIP5K1α expression by 78.6% in PC-3 cells[1]. ISA-2011B leads to a remarkable reduction in AR-V7 and CDK1 in both nucleus and cytoplasm of 22Rv1 cells. ISA-2011B treatment also abolishes AR expression in the nucleus, without depleting the cytoplasmic AR[2].
In Vivo	ISA-2011B significantly inhibits growth of tumor cells in xenograft mice, and is mediated by targeting PIP5K1α-associated PI3K/AKT and the downstream survival, proliferation, and invasion pathways[1]. Overexpression of AR-V7 increases PIP5K1α, promotes rapid growth of PCa in xenograft mice, whereas inhibition of PIP5K1α by its inhibitor ISA-2011B suppresses the growth and invasiveness of xenograft tumors overexpressing AR-V7. ISA-2011B disrupts protein stabilization of AR-V7 which is dependent on PIP5K1α, leading to suppression of invasive growth of AR-V7-high tumors in xenograft mice[2].

Solvent&Solubility

In Vitro:

DMSO : 100 mg/mL (**235.93 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3593 mL	11.7966 mL	23.5933 mL
	5 mM	0.4719 mL	2.3593 mL	4.7187 mL
	10 mM	0.2359 mL	1.1797 mL	2.3593 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 (5.90 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.90 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 (5.90 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.90 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 (5.90 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.90 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]. Semenas J, et al. The role of PI3K/AKT-related PIP5K1α and the discovery of its selective inhibitor for treatment of advanced prostate cancer. Proc Natl Acad Sci U S A. 2014 Sep 2;111(35):E3689-98. [2]. Sarwar M, et al. Targeted suppression of AR-V7 using PIP5K1α inhibitor overcomes enzalutamide resistance in prostate cancer cells. Oncotarget. 2016 Sep 27;7(39):63065-63081.

实验参考：

Cell Assay	Cells are grown in phenol red-free RPMI-1640 medium 24 hours and then are treated with drugs alone or in combination for 24 hours or 48 hours. Enzalutamide at 5 μM or ISA-2011B at 20 μM or 50 μM final concentrations or solvent DMSO 1% is used. For treatment of 22Rv1 cells with MG132, a proteasome inhibitor, cells are treated with MG132 at 1 μM. For combination treatment of MG132 and ISA-2011B, cells are pre-treated with MG132 for 30 min at 1 μM prior to treatment of ISA-2011B[2].
Animal Administration	Mice: BALB/c nude mice aged 8 to 12 wk are used in the experiments. Tumor cells are implanted into the mice. Tumor xenografts are treated with vehicle (control), docetaxel (10 mg/kg), ISA-2011B (40 mg/kg), and docetaxel (10 mg/kg) in combination with ISA-2011B (40 mg/kg) every second day[1].
References	[1]. Semenas J, et al. The role of PI3K/AKT-related PIP5K1α and the discovery of its selective inhibitor for treatment of advanced prostate cancer. Proc Natl Acad Sci U S A. 2014 Sep 2;111(35):E3689-98. [2]. Sarwar M, et al. Targeted suppression of AR-V7 using PIP5K1α inhibitor overcomes enzalutamide resistance in prostate cancer cells. Oncotarget. 2016 Sep 27;7(39):63065-63081.