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产品名称：ARV-771
产品别名：ARV-771

生物活性：

Description	ARV-771 is a potent BET degrader based on PROTAC technology with K_ds of 34, 4.7, 8.3, 7.6, 9.6, and 7.6 nM for BRD2(1), BRD2(2), BRD3(1), BRD3(2), BRD4(1), and BRD4(2), respectively[1].

IC_{50} & Target	BRD2(1)	BRD2(2)	BRD3(1)	BRD3(2)	BRD4(1)	BRD4(2)
	34 nM (Kd)	4.7 nM (Kd)	8.3 nM (Kd)	7.6 nM (Kd)	9.6 nM (Kd)	7.6 nM (Kd)

In Vitro	ARV-771, a small-molecule pan-BET degrader based on proteolysis-targeting chimera (PROTAC) technology, demonstrates dramatically improved efficacy in cellular models of CRPC as compared with BET inhibition. ARV-771 potently degrades BRD2/3/4 in 22Rv1 cells with a DC_{50} less than 5 nM. c-MYC protein is a downstream effector of BET proteins. Treatment with ARV-771 results in depletion of c-MYC with an IC_{50} of less than 1 nM. ARV-771 shows strong antiproliferative effect on 22Rv1, VCaP, and LnCaP95 cell lines. ARV-771 treatment has a pronounced effect on cell morphology consistent with apoptosis. FL-AR and AR-V7 mRNA are down-regulated upon treatment with 10 nM ARV-771 in VCaP cells. ARV-771 has an antiandrogenic effect on a number of AR-regulated genes in VCaP cells[1].
In Vivo	Treatment of non castrated male Nu/Nu mice bearing AR-V7+ 22Rv1 tumor xenografts with daily subcutaneous injections of ARV-771 at 10 mg/kg for 3 d results in 37% and 76% down-regulation of BRD4 and c-MYC levels, respectively, in tumor tissue. A marked down-regulation in levels of AR-V7 is observed in the 22Rv1 tumors after ARV-771 treatment[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (50.68 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.0135 mL	5.0677 mL	10.1354 mL
	5 mM	0.2027 mL	1.0135 mL	2.0271 mL
	10 mM	0.1014 mL	0.5068 mL	1.0135 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 (2.53 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (2.53 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 (2.53 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (2.53 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 (2.53 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (2.53 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]. Raina K, et al. PROTAC-induced BET protein degradation as a therapy for castration-resistant prostate cancer. Proc Natl Acad Sci U S A. 2016 Jun 28;113(26):7124-9.

实验参考：

Cell Assay	ARV-771 is dissolved in DMSO. 22Rv1 cells (5,000 cells per well) are dosed with ARV-771 serially diluted 1:3 for a 10-point dose curve for 72 h. CellTiter-Glo Luminescent Cell Viability Assay is added, and the plate is read on a luminometer. Data are analyzed and plotted using GraphPad Prism software[1].
Animal Administration	Mice: Mice bearing tumors are treated with ARV-771 (5, 10, 30, 50 mg/kg) for up to 3 wk, depending on the experiment. Mice are sacrificed 8 h after the final dose. Plasma and tissues are harvested and flash frozen for further analysis[1].
References	[1]. Raina K, et al. PROTAC-induced BET protein degradation as a therapy for castration-resistant prostate cancer. Proc Natl Acad Sci U S A. 2016 Jun 28;113(26):7124-9.