

产品名称：**ARN-509**
产品别名：**Apalutamide**

生物活性:				
Description	Apalutamide (ARN-509) is a potent and competitive androgen receptor (AR) antagonist, binding AR with an IC ₅₀ of 16 nM.			
IC ₅₀ & Target	IC50: 16 nM (Androgen receptor)[1]			
In Vitro	Apalutamide (ARN-509) also exhibits low micromolar affinity (IC ₅₀ 3 μM) for the GABA _A receptor in radioligand binding-assays and thus may potentially antagonize GABA _A at therapeutic dose levels[1]. Apalutamide is a potent androgen receptor (AR) antagonist that targets the AR ligand-binding domain and prevents AR nuclear translocation, DNA binding, and transcription of AR gene targets[2].			
In Vivo	Apalutamide (ARN-509) exhibits low systemic clearance, high oral bioavailability and long plasma half-life in both mouse and dog, supporting once-daily oral dosing. Consistent with its long terminal-half-life, Apalutamide steady-state plasma-levels increases in repeat-dose studies, resulting in high C _{24hr} levels and low peak:trough ratios (ratio:2.5). Castrate male mice bearing LNCaP/AR xenograft tumors are treated with either Apalutamide at doses of 1, 10 or 30 mg/kg/day. Thirteen of 20 Apalutamide (30 mg/kg/day)-treated animals exhibit >50% reduction in tumor-volume at day 28 versus 3 of 19 MDV3100 (30 mg/kg/day)-treated mice[1].			
Solvent&Solubility	In Vitro: DMSO : ≥ 83.3 mg/mL (174.48 mM) H ₂ O : < 0.1 mg/mL (insoluble) * "≥" means soluble, but saturation unknown.			
	<div>Preparing Stock Solutions</div>	<div>Solvent Mass Concentration</div>	1 mg	5 mg
		1 mM	2.0945 mL	10.4727 mL
		5 mM	0.4189 mL	2.0945 mL
		10 mM	0.2095 mL	1.0473 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℃，6 months；-20℃，1 month。-80℃ 储存时，请在 6 个月内使用，-20℃ 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 (5.24 mM); Suspended solution; Need ultrasonic and warming 此方案可获得 2.5 mg/mL (5.24 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 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% corn oil			

	<p>Solubility: ≥ 2.5 mg/mL (5.24 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.24 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。</p> <p>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。</p>
References	<p>[1]. Clegg NJ, et al. ARN-509: a novel antiandrogen for prostate cancer treatment. <i>Cancer Res.</i> 2012 Mar 15;72(6):1494-503.</p> <p>[2]. Smith MR, et al. Phase 2 Study of the Safety and Antitumor Activity of Apalutamide (ARN-509), a Potent Androgen Receptor Antagonist, in the High-risk Nonmetastatic Castration-resistant Prostate Cancer Cohort. <i>Eur Urol.</i> 2016 May 6. pii: S0302-2838(16)30133</p>
实验参考:	
Cell Assay	<p>rypsinized VCaP cells are adjusted to a concentration of 100,000 cells per mL in phenol-red-free RPMI 1640 (with 5% CSS), and dispensed in 16 μL aliquots into CellBIND 384 well plates. Cells are incubated for 48 hours, after which ligand is added in a 16 μL volume to the RPMI culture medium. For the antagonist mode assay, the ligands are diluted in culture medium also containing 30 pM R1881. After 7 days' incubation, 16 μL of CellTiter-Glo Luminescent Cell Viability Assay is added and Relative Luminescence Units (RLUs) measured [1].</p>
Animal Administration	<p>Mice[1].</p> <p>In vivo xenograft experiments to determine anti-tumor response are carried out in SHO SCID male mice. Mice are orchietomized under isoflurane anesthesia and are given 2-3 days to recover prior to tumor cell injection. LNCaP/AR(cs) cells are suspended in 50% RPMI, 50% Matrigel, and 5×10^6 cells/xenograft are injected in a volume of 100 μL. Animals are observed weekly until tumor growth is apparent. From 24 d post-injection, tumors are measured weekly, and after 40-60 days post-injection, animals are randomized into cohorts of equivalent mean (150-250 mm³) and range tumor burden. All compounds (e.g., Apalutamide, 30 mg/kg per day) are administered daily by oral gavage. Statistical analyses are performed using Graphpad Prism.</p>
References	<p>[1]. Clegg NJ, et al. ARN-509: a novel antiandrogen for prostate cancer treatment. <i>Cancer Res.</i> 2012 Mar 15;72(6):1494-503.</p> <p>[2]. Smith MR, et al. Phase 2 Study of the Safety and Antitumor Activity of Apalutamide (ARN-509), a Potent Androgen Receptor Antagonist, in the High-risk Nonmetastatic Castration-resistant Prostate Cancer Cohort. <i>Eur Urol.</i> 2016 May 6. pii: S0302-2838(16)30133</p>