

产品名称：**ODM-201**
 产品别名：**Darolutamide**

生物活性:

Description	Darolutamide (ODM-201;BAY-1841788) is a potent androgen receptor (AR) antagonist with an IC₅₀ of 26 nM in <i>in vitro</i> assay.				
IC ₅₀ & Target	IC50: 26 nM (AR-HEK293 cells, AR)[1]				
In Vitro	In competitive AR binding assays, the inhibition constant (Ki) values of Darolutamide (ODM-201) are 11 nM. ODM-201and ORM-15341 suppress androgen-induced cell proliferation more efficaciously than enzalutamide or ARN-509, IC50 values being 230 and 170 nM for Darolutamide and ORM-15341 vs. 410 and 420 nM for enzalutamide and ARN-509. Darolutamide has no effect on the viability of AR-negative cell lines tested, DU-145 prostate cancer cells and H1581 lung cancer cells confirming that the antiproliferative properties of Darolutamide and ORM-15341 are specific to AR-dependent PC cells[1].				
In Vivo	Darolutamide (ODM-201) shows a significant antitumor activity with both doses, 50 mg/kg twice daily being more efficacious compared to castrated, untreated mice (p<0.001) or Enzalutamide (p=0.0245), which also shows inhibition of tumor growth (p<0.05) vs. castrated, untreated mice. Further, there is no sign of treatment-related toxicities; the body weights of mice treated with Darolutamide twice daily do not decrease significantly during the treatment[1].				
Solvent&Solubility	In Vitro: DMSO : 100 mg/mL (250.72 mM; Need ultrasonic)				
	Preparing Stock Solutions	Solvent Concentration Mass	1 mg	5 mg	10 mg
		1 mM	2.5072 mL	12.5360 mL	25.0721 mL
		5 mM	0.5014 mL	2.5072 mL	5.0144 mL
		10 mM	0.2507 mL	1.2536 mL	2.5072 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 (6.27 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.27 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 (6.27 mM); Clear solution				

	此方案可获得 ≥ 2.5 mg/mL (6.27 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 生理盐水溶液中, 混合均匀。 3.请依序添加每种溶剂: 10% DMSO $\rightarrow$ 90% corn oil Solubility: ≥ 2.5 mg/mL (6.27 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.27 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]. Moilanen AM, et al. Discovery of ODM-201, a new-generation androgen receptor inhibitor targeting resistance mechanisms to androgen signaling-directed prostate cancer therapies. Sci Rep. 2015 Jul 3;5:12007. doi: 10.1038/srep12007.
实验参考:	
Cell Assay	To study the antiproliferative properties of Darolutamide and ORM-15341, the VCaP cell line originally derived from a bone metastasis of a CRPC patient is used. The VCaP cell line is characterized with endogenous AR gene amplification and AR overexpression³⁰, typical for CRPC. VCaP cells are cultured in RPMI-1640 medium and supplemented with 10% fetal bovine serum (FBS), 100 UI/mL penicillin, 100 μg/mL streptomycin, and 4 mM VCaP[1].
Animal Administration	To elucidate the in vivo efficacy of Darolutamide in a CRPC mouse model, castrated male nude mice with subcutaneously injected VCaP cells are treated orally with ODM-201 (50 mg/kg) once (qd) or twice daily (bid), or with enzalutamide (20 mg/kg, qd) for 37 days. The dose for enzalutamide is selected based on previously published studies⁹ and our pharmacokinetic (PK) analyses which reveals that in mice the systemic exposure (AUC₀₋₂₄) for this dose of enzalutamide is 2.5 times higher than that for Darolutamide (50 mg/kg, bid). Moreover, enzalutamide exhibited a long plasma half-life (18.3 hours) while the half-life of Darolutamide in mice is not optimal (1.6 hours) supporting once daily dosing for enzalutamide and higher dose and more frequent dosing for ODM-201[1].
References	[1]. Moilanen AM, et al. Discovery of ODM-201, a new-generation androgen receptor inhibitor targeting resistance mechanisms to androgen signaling-directed prostate cancer therapies. Sci Rep. 2015 Jul 3;5:12007. doi: 10.1038/srep12007.