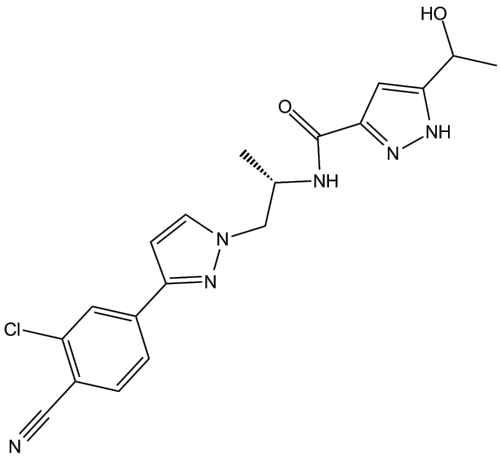
Product Data Sheet

Product Name: ODM-201
Cat. No.: GC11386

Chemical Properties

Cas. No.	1297538-32-9		
Chemical Name	N-((S)-1-(3-(3-chloro-4-cyanophenyl)-1H-pyrazol-1-yl)propan-2-yl)-5-(1-hydroxyethyl)-1H-pyrazole-3-carboxamide		
SMILES	N#CC1=C(Cl)C=C(C2=NN(C[C@H](C)NC(C3=NNC(C(O)C)=C3)=O)C=C2)C=C1		
Formula	$C_{19}H_{19}ClN_6O_2$	M.Wt	398.85
Solubility	≥ 19.95mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines LNCaP/AR cells

Product Data Sheet

Preparation Method	LNCaP/AR cells were cultured in RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin at 37°C in the presence of 5% CO_2. 2×10^4 cells per well were seeded in a 96-well plate for 24h, and were treated with different concentrations of ODM-201 (0.1, 1, 2, 4, 6, 8, and 10μM). After a 6-day incubation with ODM-201, cell viability was measured.
Reaction Conditions	0.1, 1, 2, 4, 6, 8, and 10μM; 6 days
Applications	ODM-201 treatment significantly reduced the cell viability of LNCaP/AR cells in a dose-dependent manner.

Animal experiment [2]:

Animal models	Male BALB/c nude mice
Preparation Method	Male BALB/c nude mice (4-week-old) were housed in temperature (23±2°C) and light-controlled (12:12-hour light-dark cycle) animal care facility. Subcutaneously inject 2×10^6 LNCaP cells into mice. When the average tumor volume reached approximately $100mm^3$, the mice were intraperitoneally injected with ODM-201 (20mg/kg/day), RSL-3 (10mg/kg/day), or vehicle. The procedure was continued for 14 days. Mice were monitored daily, and the tumor volume was calculated using the following equation: $volume=length\times width^2\times1/2$.
Dosage form	20mg/kg/day for 14 days; i.p.
Applications	ODM-201 treatment inhibited the tumor growth in mice with LNCaP cell xenografts.

Caution: Product has not been fully validated for medical applications. For research use only.
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References:
[1] Yu J, Zhou P, Hu M, et al. Discovery and biological evaluation of darolutamide derivatives as inhibitors and down-regulators of wild-type AR and the mutants[J]. European journal of medicinal chemistry, 2019, 182: 111608.
[2] Li B, Cheng B, Huang H, et al. Darolutamide-mediated phospholipid remodeling induces ferroptosis through the SREBP1-FASN axis in prostate cancer[J]. International journal of biological sciences, 2024, 20(12): 4635.

Background

ODM-201 is a potent antagonist of the androgen receptor (AR) with a Ki value of 11nM and an IC_{50} value of 26nM [1]. ODM-201 maintains the binding conformation in the F877L-mutated pocket through hydrogen and Van der Waals interactions, inhibiting transcriptional activity of AR mutants [2]. ODM-201 has been widely used in preclinical models to inhibit the progression of prostate cancer[3].

In vitro, ODM-201 treatment for 6 days significantly inhibited the viability of LNCaP/AR cells, with an IC_{50} value of 1.65μM[4]. Treatment with 10μM ODM-201 for 72 hours significantly inhibited the growth of C4-2 cells and induced cellular senescence, down-regulating the mRNA level of CDKN2A and the protein level of p16[5]. Treatment with 30μM ODM-201 for 4 days significantly reduced the expression of cyclin D1 in BT-549 cells, upregulated the phosphorylation of ERK, and inhibited cell proliferation[6].

In vivo, ODM-201 treatment via intraperitoneally injection at a dose of 20mg/kg/day for 14 days inhibited the tumor growth in mice with LNCaP cell xenografts[7]. Oral administration of 100mg/kg dose of ODM-201 daily for 2 months significantly inhibited tumor growth in the xenograft mouse model of KuCaP-1 prostate cancer carrying the AR W742C mutation, with limited weight loss[8].

References:
[1] Moilanen A M, Riikonen R, Oksala R, et al. Discovery of ODM-201, a new-generation androgen receptor inhibitor targeting resistance mechanisms to androgen signaling-directed prostate cancer therapies[J]. Scientific reports, 2015, 5(1): 12007.
[2] Borgmann H, Lallous N, Ozistanbullu D, et al. Moving towards precision urologic oncology:

targeting enzalutamide-resistant prostate cancer and mutated forms of the androgen receptor using the novel inhibitor darolutamide (ODM-201)[J]. European urology, 2018, 73(1): 4-8.
[3] Bastos D A, Antonarakis E S. Darolutamide for castration-resistant prostate cancer[J]. OncoTargets and therapy, 2019: 8769-8777.
[4] Yu J, Zhou P, Hu M, et al. Discovery and biological evaluation of darolutamide derivatives as inhibitors and down-regulators of wild-type AR and the mutants[J]. European journal of medicinal chemistry, 2019, 182: 111608.
[5] Gupta S, Pungsrinont T, Ženata O, et al. Interleukin-23 represses the level of cell senescence induced by the androgen receptor antagonists enzalutamide and darolutamide in castration-resistant prostate cancer cells[J]. Hormones and Cancer, 2020, 11(3): 182-190.
[6] Kuroiwa Y, Ito K, Nakayama J, et al. Analysis of the responsiveness to antiandrogens in multiple breast cancer cell lines[J]. Genes to Cells, 2024, 29(4): 301-315.
[7] Li B, Cheng B, Huang H, et al. Darolutamide-mediated phospholipid remodeling induces ferroptosis through the SREBP1-FASN axis in prostate cancer[J]. International journal of biological sciences, 2024, 20(12): 4635.
[8] Sugawara T, Baumgart S J, Nevedomskaya E, et al. Darolutamide is a potent androgen receptor antagonist with strong efficacy in prostate cancer models[J]. International journal of cancer, 2019, 145(5): 1382-1394.