Data Sheet (Cat.No.T212543)

TargetMol

LYA914

Chemical Properties

CAS No. :

Formula:

Molecular Weight:

Storage: Keep away from direct sunlight
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	LYA914 is an orally active AR/AR-V7 PROTAC degrader. It targets the proteolysis of the androgen receptor's (AR) conserved DNA-binding domain (DBD). LYA914 demonstrates effective antiproliferative activity in Enzalutamide-insensitive or resistant cells and inhibits tumor growth in VCaP/LNCaP tumor mouse models. It is suitable for studying castration-resistant prostate cancer (CRPC).
Targets(IC50)	Androgen Receptor,Akt,PROTACs
In vitro	LYA914, within a concentration range of 1-10 μM, degrades AR protein in LNCaP and 22Rv1 cells, achieving degradation rates of 40.2% and 39.1% at 1 μM, and 82.5% and 84.5% at 10 μM, respectively. It also degrades AR-V7 protein in 22Rv1 cells, with degradation rates of 37.4% at 1 μM and 83.9% at 10 μM. LYA914 (0.01-10 μM, 24 h) enhances CRBN and AR binding, induces degradation of AR and AR-V7, with DC50 values in 22RV1 cells of 0.41 and 0.83 μM, and in VCaP cells of 0.32 and 0.33 μM, also inducing degradation of AR and AR-V7 in LNCaP cells. LYA914 (24 hours) inhibits AR or AR-V7 overexpression and AR/AR-V7-driven transcriptional activity in 293T cells, with IC50 values of 0.19 and 1.29 μM. In 22Rv1 cells, LYA914 (1-3 μM, 48 hours) significantly inhibits the AR/AR-V7 signaling pathway through transcriptional repression. Over 5 days, LYA914 exhibits antiproliferative activity in LNCaP, VCaP, and 22Rv1 cells, with IC50 values of 1.21, 1.6, and 1.15 μM, and shows low cytotoxicity towards HL-7702 cells. LYA914 (6 days) maintains antiproliferative effects on LNCaP-EN and VCaP-EN cells after enzalutamide exposure, with IC50 values of 4.12 and 1.66 μM. Furthermore, LYA914 (24 hours) significantly inhibits the transcriptional activity in HEK293T cells co-transfected with AR reporter plasmids and either AR (F876L) or AR (W741L) plasmids, with IC50 values of 1.29 and 0.53 μM, respectively.
In vivo	LYA914, when administered via intraperitoneal injection at doses of 30-100 mg/kg once daily for 3 weeks, inhibits tumor growth in the LNCaP tumor model by downregulating AR protein expression. Additionally, LYA914 shows notable oral efficacy in inhibiting tumor growth in the VCaP xenograft model at doses of 10-30 mg/kg once daily for 16 days. Furthermore, LYA914, administered orally at 30-60 mg/kg once daily for 14 days, demonstrates good tolerance without signs of toxicity in ICR mice.

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