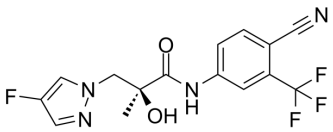
UT-34

Cat. No.:	HY-136242
CAS No.:	2168525-92-4
Molecular Formula:	$C_{15}H_{12}F_4N_4O_2$
Molecular Weight:	356.27
Target:	Androgen Receptor
Pathway:	Others
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (701.72 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8069 mL	14.0343 mL	28.0686 mL
	5 mM	0.5614 mL	2.8069 mL	5.6137 mL
	10 mM	0.2807 mL	1.4034 mL	2.8069 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.84 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.84 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.84 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

UT-34 is a potent, selective and orally active second-generation pan-androgen receptor (AR) antagonist and degrader with IC_{50}s of 211.7 nM, 262.4 nM and 215.7 nM for wild-type, F876L and W741L AR, respectively. UT-34 binds to ligand-binding domain (LBD) and function-1 (AF-1) domains and requires ubiquitin proteasome pathway to degrade the AR. UT-34 has anti-prostate cancer efficacy[1][2].

IC_{50} & Target

IC50: 211.7 nM (Wild-type AR), 262.4 nM (F876L AR) and 215.7 nM (W741L AR)[1]

In Vitro

UT-34 (3-10 μM; 24 hours; LNCaP cells) treatment inhibits the expression of PSA and FKBP5 and growth of LNCaP cells starting from 100 nM with maximum effect observed at 10 μM[1].
UT-34 (0.1-10 μM; 24 hours; LNCaP cells) treatment results in a reduction of AR levels at 1000 nM in LNCaP cells[1].
Treatment of ZR-75-1 cells maintained in serum-containing growth medium with UT-34 results in downregulation of AR protein levels, but not estrogen receptor (ER) or progesterone receptor (PR) levels. Furthermore, in MDA-MB-453 breast cancer cells that express AR and glucocorticoid receptor (GR), UT-34 induces the downregulation of AR, but not GR[1].
UT-34 is an effective degrader of both AR and AR-V7. LNCaP-ARV7 cells are treated for 24 hours in the presence of 0.1 nM R1881 or 10 ng/mL Doxycycline. Doxycycline induces the expression of EDN2, which is inhibited by UT-34, while UT-34 inhibits the expression of R1881-induced FKBP5 gene expression[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	LNCaP cells
Concentration:	3 μM, 10 μM
Incubation Time:	24 hours
Result:	Inhibited the expression of PSA and FKBP5 and growth of LNCaP cells starting from 100 nM with maximum effect observed at 10 μM.

Western Blot Analysis[1]

Cell Line:	LNCaP cells
Concentration:	0.1 μM, 1 μM, 10 μM
Incubation Time:	24 hours
Result:	Resulted in a reduction of AR levels at 1000 nM.

In Vivo

UT-34 (20-40 mg/kg; oral administration; daily; for 14 days; NSG mice) at 20 and 40 mg/kg reduces the seminal vesicle weight by 10%-20% and 50%-60 %, respectively[1].
UT-34 inhibits androgen-dependent tissues such as prostate and seminal vesicles in rats, and the growth of Enzalutamide-resistant castration-resistant prostate cancer (CRPC) xenografts. UT-34 also induces tumor regression in intact immunocompromised rats[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Non obese diabetic/severe combined immunodeficiency Gamma (NSG) mice injected with MR49F cells[1]
Dosage:	20 mg/kg or 40 mg/kg
Administration:	Oral administration; daily; for 14 days
Result:	Reduced the seminal vesicle weight.

REFERENCES

[1]. Ponnusamy S, et al. Orally Bioavailable Androgen Receptor Degrader, Potential Next-Generation Therapeutic for Enzalutamide-Resistant Prostate Cancer. Clin Cancer Res. 2019 Nov 15;25(22):6764-6780.

[2]. Stone L. UT-34: a promising new AR degrader. Nat Rev Urol. 2019 Nov;16(11):640.

Caution: Product has not been fully validated for medical applications. For research use only.

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