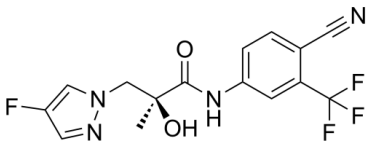
Data Sheet

Product Name:	UT-34
Cat. No.:	CS-0120977
CAS No.:	2168525-92-4
Molecular Formula:	$C_{15}H_{12}F_4N_4O_2$
Molecular Weight:	356.27
Target:	Estrogen Receptor/ERR
Pathway:	Vitamin D Related/Nuclear Receptor
Solubility:	DMSO : 250 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

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**, belonging to Ligands for Target Protein for PROTAC. UT-34 has anti-prostate cancer efficacy[1][2]. IC50 & 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]. ***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].

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.

CAIndexNames:

1H-Pyrazole-1-propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-4-fluoro-α-hydroxy-α-methyl-, (αS)-

SMILES:

O=C(NC1=CC=C(C#N)C(C(F)(F)F)=C1)[C@@](C)(O)CN2N=CC(F)=C2

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

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