

## Product Data Sheet

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Product Name: PROTAC AR Degradar-12

Cat. No.: GC81303

### Chemical Properties

Cas. No.

Formula  $C_{57}H_{76}N_8O_{10}S$  M.Wt 1065.33

Solubility DMSO: 100 mg/mL (93.87 mM; Need ultrasonic) 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.

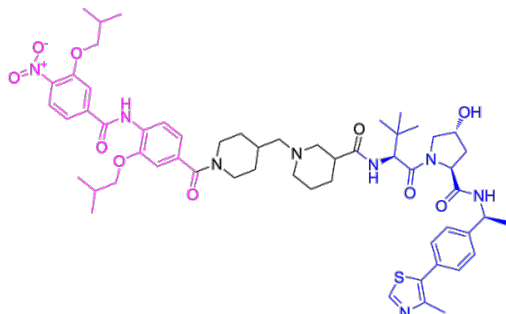
**Caution: Product has not been fully validated for medical applications. For research use only.**

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### Structure



### Background

PROTAC AR Degradar-12 is a highly efficient PROTAC targeting AR coactivator binding site (AR-CBS). PROTAC AR Degradar-12 induces AR degradation in a ubiquitin proteasome system (UPS) pathway-dependent manner. PROTAC AR Degradar-12 inhibits tumor cell growth by affecting DNA replication and cell division. PROTAC AR Degradar-12 could not only effectively degrade AR, but also potentially inhibit the proliferation of MCF-7 and multiple mutant or resistant BC cells. PROTAC AR Degradar-12 effectively blocked estrogen receptor  $\alpha$  (ER $\alpha$ ) signaling through a dual mechanism involving ER $\alpha$  protein downregulation and suppression of its transcriptional activity. PROTAC AR Degradar-12 significantly inhibits the mRNA expression of FOXA1, GREB1, SRC, and PELP1. PROTAC AR Degradar-12 can be used for the study of breast cancer [1]. (Pink: AR ligand; Blue: VHL ligand; Black: linker).

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In Vivo, PROTAC AR Degradar-12 (Compound 18o) (5-10  $\mu\text{M/kg}$ , i.p., once every other day) significantly inhibits tumor growth in MCF-7 cells and LCC2 cells xenograft mice, promotes AR protein degradation and ER $\alpha$  signaling inhibition, without weight loss or other toxicities<sup>[1]</sup>.

In Vitro, PROTAC AR Degradar-12 (Compound 18o) shows good inhibitory activity against MCF-7 ( $\text{IC}_{50} = 0.13 \mu\text{M}$ ) and LCC2 cells ( $\text{IC}_{50} = 0.54 \mu\text{M}$ ) and exhibits broad-spectrum efficacy against clinically relevant mutant variants, demonstrating potent submicromolar inhibition of MCF-7D538G ( $\text{IC}_{50} = 0.66 \mu\text{M}$ ), MCF-7Y537S ( $\text{IC}_{50} = 0.44 \mu\text{M}$ ), and MCF-7EGFR ( $\text{IC}_{50} = 0.52 \mu\text{M}$ )<sup>[1]</sup>. PROTAC AR Degradar-12 (0.01-2  $\mu\text{M}$ , 24 h) effectively and in a dose-dependent manner degrades AR protein in MCF-7 cells ( $\text{DC}_{50} = 0.72 \mu\text{M}$ )<sup>[1]</sup>. PROTAC AR Degradar-12 (1  $\mu\text{M}$ , 0-24 h) shows a time-dependent effect on AR degradation in MCF-7 cells<sup>[1]</sup>. PROTAC AR Degradar-12 (0.01-2  $\mu\text{M}$ , 24 h) causes a concentration-dependent downregulation of ER $\alpha$  protein in MCF-7 cells<sup>[1]</sup>. PROTAC AR Degradar-12 (0.01-2  $\mu\text{M}$ , 12-24 h) significantly downregulates ER $\alpha$  protein in MCF-7D538G, MCF-7Y537S, MCF-7EGFR, LCC2, and T47D cells, and fails to downregulate ER $\beta$  protein in PC9 cells<sup>[1]</sup>. PROTAC AR Degradar-12 (1  $\mu\text{M}$ , 24 h) induces a decrease in ER $\alpha$  through an indirect mechanism, rather than by directly targeting the degradation of CBS in MCF-7 cells<sup>[1]</sup>. PROTAC AR Degradar-12 (0-5  $\mu\text{M}$ , 0-24 h) reduces AR protein in MCF-7 cells due to posttranscriptional degradation, while the reduction in ER $\alpha$  was a result of transcriptional repression<sup>[1]</sup>. PROTAC AR Degradar-12 exhibits potent antiproliferative activity in AR-overexpressing but ER $\alpha$ -deficient prostate cancer cells LNCaP ( $\text{IC}_{50} = 0.46 \mu\text{M}$ ), while its antiproliferative activity is significantly reduced in AR-negative MDA-MB-231 cells ( $\text{IC}_{50} > 30 \mu\text{M}$ )<sup>[1]</sup>. PROTAC AR Degradar-12 was very effective in stabilizing the AR protein at high temperature, while it only displays a weak protective effect on ER $\alpha$  protein, suggesting that compound PROTAC AR Degradar-12 engages AR but does not bind to ER $\alpha$  in LCC2 cells<sup>[1]</sup>. PROTAC AR Degradar-12 (1  $\mu\text{M}$ , 24 h) significantly inhibits the mRNA expression of FOXA1, GREB1, SRC, and PELP1 in MCF-7 cells<sup>[1]</sup>. PROTAC AR Degradar-12 (1-10  $\mu\text{M}$ , 48 h) induces S-phase cell cycle arrest in MCF-7 and LCC2 cells<sup>[1]</sup>.

### References:

[1]. Wu Y, et al. Kill Two Birds with One Stone: An Efficient and Potent AR CBS-Targeted Degradar Reverses Breast Cancer Resistance via Concurrent AR Degradation and ER $\alpha$  Transcriptional

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