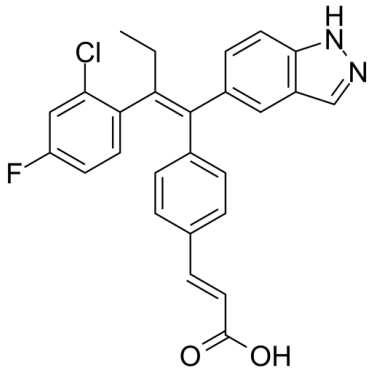
Data Sheet

Product Name:	Brilanestrant
Cat. No.:	CS-4588
CAS No.:	1365888-06-7
Molecular Formula:	C26H20ClFN2O2
Molecular Weight:	446.90
Target:	Estrogen Receptor/ERR
Pathway:	Others
Solubility:	DMSO : ≥ 30 mg/mL (67.13 mM)



BIOLOGICAL ACTIVITY:

Brilanestrant (ARN-810; GDC-0810) is an orally bioavailable **selective estrogen receptor degrader (SERD)** with **IC_{50}** of 0.7 nM. IC50 & Target: IC50: 0.7 nM (estrogen receptor) **In Vitro:** Brilanestrant (ARN-810; GDC-0810) is a potent ER-α binder (IC_{50}=6.1 nM), a full transcriptional antagonist with no agonism (3× ERE, IC_{50}=2 nM), and displays good potency and efficacy in ER-α degradation (EC_{50} =0.7 nM) and MCF-7 breast cancer cell viability (IC_{50}=2.5 nM) assays[1].Brilanestrant (ARN-810; GDC-0810) induces a distinct ERα conformation versus tamoxifen and other ER therapeutics, and does not exhibit tamoxifen-like ER agonism in MCF7 cells[2]. **In Vivo:** The pharmacokinetic profile of Brilanestrant (ARN-810) shows it is a olw clearance molecule across species, with good bioavailability (40%-60%). Brilanestrant (ARN-810) (3 mg/kg, p.o.) shows substantial tumor-growth inhibition in a tamoxifen-sensitive MCF-7 xenograft model, while at the highest dose of 100 mg/kg/day, all animals show tumor regression of more than 50% without weight loss[1].

Brilanestrant (ARN-810) exhibits low clearance (11 mL/min/kg) and 61% oral bioavailability. Brilanestrant (ARN-810) (1-100 mg/kg/day, p.o.) displays dose dependent efficacy in the MCF7 xenograft model[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]MCF-7 cells are adjusted to a concentration of 40000 cells per mL in RPMI containing 10% FBS and 20 mM HEPES. Then 16 µL of the cell suspension (640 cells) is added to each well of a 384-well plate, and the cells are incubated overnight to allow the cells to adhere. The following day a 10-point, serial 1:5 dilution of each compound is added to the cells in 16 µL at a final concentration ranging from 10 to 0.000005 µM. After 5 days' compound exposure, 16 µL of CellTiter-GLo is added to the cells, and the relative luminescence units of each well are determined. CellTiter-GLo added to 32 µL of medium without cells is used to obtain a background value. The percent viability of each sample is determined as follows: (RLU sample-RLU background/RLU untreated cells-RLU background ×100=%viability) **Animal Administration:** [1]Time release pellets containing 0.72 mg 17-β estradiol are subcutaneously implanted into nu/nu mice. MCF-7 cells are grown in RPMI containing 10% FBS at 5% CO_2 37°C. Trypsinized cells are pelleted and resuspended in 50% RPMI (serum free) and 50% Matrigel at $1×10^7$ cells/mL. MCF-7 cells are subcutaneously injected (100 µL/animal) on the right flank 2-3 days post pellet implantation. Tumor volume (length × $width^2/2$) is monitored biweekly. When tumors reach an average volume of appr 200 mm^3 animals are randomized and treatment is started. Animals are treated with vehicle or compound daily for 4 weeks. Tumor volume and body weight are monitored biweekly throughout the study.

References:

[1]. By Lai, et al. Identification of GDC-0810 (ARN-810), an Orally Bioavailable Selective Estrogen Receptor Degrader (SERD) that Demonstrates Robust Activity in Tamoxifen-Resistant Breast Cancer Xenografts. J Med Chem. 2015 Jun 25;58(12):4888-904.

[2]. Joseph JD, et al. The selective estrogen receptor downregulator GDC-0810 is efficacious in diverse models of ER+ breast cancer. Elife. 2016 Jul 13;5. pii: e15828. doi: 10.7554/eLife.15828

CAIndexNames:

2-Propenoic acid, 3-[4-[(1E)-2-(2-chloro-4-fluorophenyl)-1-(1H-indazol-5-yl)-1-buten-1-yl]phenyl]-, (2E)-

SMILES:

O=C(O)/C=C/C1=CC=C(/C(C2=CC3=C(NN=C3)C=C2)=C(C4=CC=C(F)C=C4Cl)/CC)C=C1

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