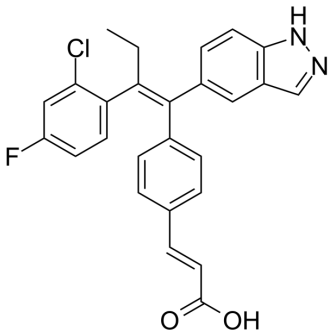
Brilanestrant

Cat. No.:	HY-12864
CAS No.:	1365888-06-7
Molecular Formula:	$C_{26}H_{20}ClFN_2O_2$
Molecular Weight:	447
Target:	Estrogen Receptor/ERR
Pathway:	Vitamin D Related/Nuclear Receptor
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (223.71 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2371 mL	11.1857 mL	22.3714 mL
	5 mM	0.4474 mL	2.2371 mL	4.4743 mL
	10 mM	0.2237 mL	1.1186 mL	2.2371 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: ≥ 2.5 mg/mL (5.59 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.59 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.65 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description	Brilanestrant (ARN-810; GDC-0810) is an orally bioavailable selective estrogen receptor degrader (SERD) with IC_{50} of 0.7 nM.
IC_{50} & 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

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) MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Mol Cancer Ther. 2020 Jul;19(7):1395-1405.
- Breast Cancer Res Treat. 2020 Jan;179(1):67-77.
- Horm Cancer. 2017 Jun;8(3):135-142.
- Harvard University. 2023 Mar. 30487357.

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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

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

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