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产品名称：GDC-0810
产品别名：Brilanestrant； ARN-810

生物活性：

Description	Brilanestrant (ARN-810; GDC-0810) is an orally bioavailable selective estrogen receptor degrader (SERD) with IC50 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].
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].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 30 mg/mL (67.13 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2376 mL	11.1882 mL	22.3764 mL
5 mM	0.4475 mL	2.2376 mL	4.4753 mL
10 mM	0.2238 mL	1.1188 mL	2.2376 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

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

实验参考：

	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

Cell Assay	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) [1]
Animal Administration	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. [1]
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