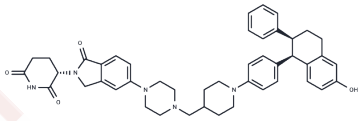
Data Sheet (Cat.No.T39710)

TargetMol

Vepdegestrant

Chemical Properties



CAS No. : 2229711-68-4

Formula: C45H49N5O4

Molecular Weight: 723.9

Storage: Keep away from direct sunlight
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Vepdegestrant (ARV-471) is a selective and highly potent estrogen receptor (ER, ESR1) PROTAC degrader with strong degrading activity against the ER protein. By directly degrading the ER protein rather than merely antagonizing its activity, vepdegestrant effectively inhibits the ER signaling pathway and demonstrates significant antitumor activity in ER-positive (ER^+) breast cancer, with a DC50 value of approximately 2 nM. It is particularly effective against tumors harboring ESR1 mutations.
Targets(IC50)	Estrogen Receptor/ERR,PROTACs
In vitro	**Methods**: MCF7 cells were treated with 100 nM Vepdegestrant for 0-24 hours, followed by Western blot analysis to detect ER expression. **Results**: ER degradation occurred rapidly, with >80% ER degraded within 4 hours. [1]
In vivo	**Methods**: MCF7 breast cancer cells were orthotopically transplanted into mice. Vepdegestrant (10 mg/kg/day) was administered orally once daily for 3 consecutive days. The mice were euthanized 18 hours after dosing, and tumor tissue was collected for Western blot analysis of ER levels. **Results**: Vepdegestrant caused a ≥90% reduction in intratumoral ER levels. [1] **Methods**: MCF7, T47D, and other ER+ breast cancer cells were treated with Vepdegestrant (ARV-471) and stimulated with 10 ng/mL IFN-γ for 24 hours; cell surface MHC-I expression was detected by flow cytometry. **Results**: As a novel selective estrogen receptor degrader (SERD), vepdegestrant significantly reversed the inhibitory effect of estrogen on IFN-γ-induced MHC-I expression and effectively upregulated the levels of key antigen-presenting molecules. [2]

Solubility Information

Solubility	DMSO: 15.28 mg/mL (21.11 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 3.3 mg/mL (4.56 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and*

In vivo Formulation	*used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.3814 mL	6.907 mL	13.8141 mL
5 mM	0.2763 mL	1.3814 mL	2.7628 mL
10 mM	0.1381 mL	0.6907 mL	1.3814 mL
50 mM	0.0276 mL	0.1381 mL	0.2763 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Gough SM, et al. Oral Estrogen Receptor PROTAC Vepdegestrant (ARV-471) Is Highly Efficacious as Monotherapy and in Combination with CDK4/6 or PI3K/mTOR Pathway Inhibitors in Preclinical ER+ Breast Cancer Models. Clin Cancer Res. 2024 Aug 15;30(16):3549-3563.

Choi H I, Choi J, Kim J W, et al.Stability Evaluation and Pharmacokinetic Profiling of Vepdegestrant in Rodents Using Liquid Chromatography–Tandem Mass Spectrometry.Molecules.2024, 29(17): 4048.

Hermida-Prado F, et al. Endocrine Therapy Synergizes with SMAC Mimetics to Potentiate Antigen Presentation and Tumor Regression in Hormone Receptor-Positive Breast Cancer. Cancer Res. 2023 Oct 2;83(19):3284-3304.

Wang C, et al. Developments of CRBN-based PROTACs as potential therapeutic agents. Eur J Med Chem. 2021 Dec 5;225:113749.