Product Datasheet

AZD9496

Catalog No. **BP-01916** · CAS **1639042-08-2** · Form **free base** · Physical state **solid** · Color **light yellow to brown** · Version **1.0** · Revision **2026-09-04**

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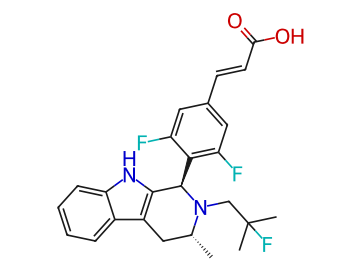
Target	Research area
Estrogen Receptor/ERR	**Cancer**

Molecular formula	$C_{25}H_{25}F_3N_2O_2$
Molecular weight	**442.4734**

STRUCTURE



DESCRIPTION

AZD9496 is a potent and selective estrogen receptor (ERα) antagonist with an IC50 of 0.28 nM. AZD9496 is an orally bioavailable selective oestrogen receptor degrader (SERD).

BIOLOGICAL ACTIVITY

In Vitro

The potency of AZD9496 with IC50 of 0.82 nM, 0.14 nM, and 0.28 nM in ERα binding, downregulation, and antagonism, respectively. AZD9496 significantly inhibits MCF-7 cell growth with EC50 of 0.04 nM[1]. Selectivity of AZD9496 over other tested nuclear hormone receptors is high: androgen receptor (AR), IC50=30 μM; glucocorticoid receptor (GR), IC50=9.2 μM; progesterone receptor (PR), IC50=0.54 μM.

In Vivo

Significant tumor growth inhibition is observed as low as 0.5 mg/kg dose in the estrogen-dependent MCF-7 xenograft model, where this effect is accompanied by a dose-dependent decrease in PR protein levels, demonstrating potent antagonist activity. Combining AZD9496 with PI3K pathway and CDK4/6 inhibitors lead to further growth-inhibitory effects compared with monotherapy alone. AZD9496, given once daily orally at 5 and 25 mg/kg produced statistically significant increases in uterine weight compared with the ICI 182780 control ($P<0.001$) but significantly lower than ICI 47699 ($P=0.001$). AZD9496 is also tested in a long-term estrogen deprived model (LTED), using the HCC-1428 LTED cell line that grows in the absence of estrogen and is thought to best represent a model of aromatase inhibition. AZD9496 shows significant activity, with a dose of 5 mg/kg giving tumor regressions in this model.

SOLUBILITY

Soluble in DMSO

REFERENCES

[1]. Weir HM, et al. AZD9496: An Oral Estrogen Receptor Inhibitor That Blocks the Growth of ER-Positive and ESR1-Mutant Breast Tumors in Preclinical Models. Cancer Res. 2016 Jun 1;76(11):3307-18.

[2]. De Savi C, et al. Optimization of a Novel Binding Motif to (E)-3-(3,5-Difluoro-4-((1R,3R)-2-(2-fluoro-2-methylpropyl)-3-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)phenyl)acrylic Acid (AZD9496), a Potent and Orally Bioavailable Selective Estrogen Receptor Downregulator and Antagonist. J Med Chem. 2015 Oct 22;58(20):8128-40.

[3]. 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.