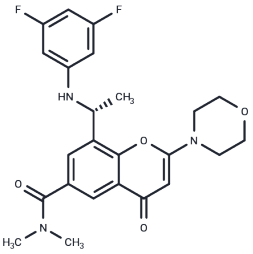
Data Sheet (Cat.No.T6773)

TargetMol

AZD8186

Chemical Properties



CAS No. : 1627494-13-6

Formula: C24H25F2N3O4

Molecular Weight: 457.47

Storage: 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	AZD8186 is an effective and specific PI3Kβ/δ inhibitor (IC50: 4/12 nM).
Targets(IC50)	PI3K
In vitro	AZD8186 potently inhibits p-Akt in MDA-MB-468 cells sensitive to PI3Kβ inhibition and Jeko B cells sensitive to PI3Kδ inhibition with IC50 of 3 nM and 4 nM, respectively. [1] AZD8186 shows preferred growth inhibition activity in most PTEN deficient cell lines with GI50 of <1 μM. [2]
In vivo	In nude mice bearing PTEN-deficient PC3 prostate tumor xenografts, AZD8186 (100 mg/kg, p.o.) strongly inhibits Akt phosphorylation levels, and causes significant tumor growth inhibition. When used in combination with ABT, AZD8186 (60 mg/kg, p.o.) results in complete inhibition of tumor growth. [1] In the mouse PTEN-null TNBC models HCC70 and MDA-MB-468, and the prostate models HID28, AZD8186 (50 mg/kg, p.o.) also inhibits the growth of tumors. [2] Combination therapy using AZD8186 with androgen deprivation results in long-lasting tumor regression, which persisted after treatment cessation. [3]
Kinase Assay	PI3Kα, PI3Kβ, PI3Kγ and PI3Kδ enzyme assays: The inhibition of PI3Kα, PI3Kβ, PI3Kγ and PI3Kδ human recombinant PI3K isoforms is evaluated using a Kinase-Glo Plus Assay Kit. 12 point half-log concentration-response curves with a top concentration of 100 μM are constructed by dispensing DMSO solubilised compounds into white 384-well medium-binding microplates using an Echo 555. 3 μL of the appropriate PI3K? in Tris buffer (50 mM Tris pH7.4, 0.05% CHAPS, 2.1 mM DTT, and 10 mM MgCl2) is added. The plate is covered and allowed to pre-incubate with compound for 20 minutes prior to addition of 3 μL of substrate solution containing PIP2 and ATP. The enzyme reaction is stopped after 80 minutes by the addition of Kinase Glo detection solution. Plates are covered and incubated for 30 minutes at room temperature before the luminescence signal is read using a PHERAstar plate reader. The final concentrations of DMSO, ATP and PIP2 in the assay are 2%, 8 μM, and 80 μM respectively. The final concentrations of PI3Kα, PI3Kβ, PI3Kγ and PI3Kδ are respectively 20 nM, 20 nM, 45 nM and 30 nM. For PI3Kα, PI3Kβ and PI3Kδ the concentration of active enzyme is determined as outlined in the enzyme assay tight binding limit determination section. For PI3Kγ the concentration of enzyme is determined by Bradford assay. IC50 values are calculated using Genedata Screener.

Cell Research	Cells are seeded in 96-well plates, at a density to allow for logarithmic growth during the 72 hour assay, and incubated overnight at 37°C, 5% CO2. Cells are treated with AZD8186 (30 to 0.003 μM) for 72 hours and cell proliferation measured by MTS. The CellTiter Aqueous Non-Radioactive Cell Proliferation Assay reagent is used in accordance with the manufacturer's protocol and Absorbance measured with Tecan Ultra instrument. Pre-dose measurements are made and the concentration needed to reduce the growth of treated cells to half that of untreated cells (GI50) values are determined.(Only for Reference)

Solubility Information

Solubility	Ethanol: 3 mg/mL (6.56 mM),Sonication is recommended. DMSO: 84 mg/mL (183.62 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 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 (7.21 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 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	2.1859 mL	10.9297 mL	21.8594 mL
5 mM	0.4372 mL	2.1859 mL	4.3719 mL
10 mM	0.2186 mL	1.093 mL	2.1859 mL
50 mM	0.0437 mL	0.2186 mL	0.4372 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

Barlaam B, et al. J Med Chem. 2015, 58(2), 943-962.
Hancox U, et al. Mol Cancer Ther. 2015, 14(1), 48-58.
Marques RB, et al. Eur Urol. 2015, 67(6), 1177-1185.