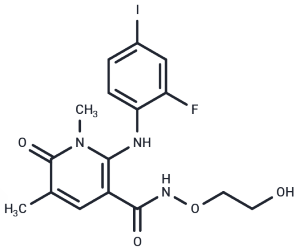
Data Sheet (Cat.No.T6083)

TargetMol

AZD8330

Chemical Properties



CAS No. : 869357-68-6

Formula: C16H17FIN3O4

Molecular Weight: 461.23

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	AZD8330 (ARRY-704) is a novel, selective, non-ATP competitive MEK 1/2 inhibitor with IC50 of 7 nM. Phase 1.
Targets(IC50)	ERK,MEK
In vitro	AZD8330 potently and strongly inhibits MEK 1/2. AZD8330 has no inhibitory activity against over 200 other kinases including at concentrations up to 10 μM. AZD8330 demonstrates sub-nanomolar potency in mechanistic (pERK) and low to sub-nanomolar potency in functional (proliferation) assays in MEK 1/2 inhibitor sensitive cell lines. [1]
In vivo	In a Calu-6 rat xenograft pharmacokinetic/pharmacodynamic (PK/PD) model a single, 1.25 mg/kg oral dose of AZD8330 inhibits ERK phosphorylation by > 90% for between 4 and 8 hours. Doses as low as 0.4 mg/kg once daily are sufficient for > 80% tumor growth inhibition in the Calu-6 nude rat xenograft model. In the Calu-6 model, AZD8330 inhibits tumor growth in a dose-dependent fashion, at 0.3 mg/kg and 1.0 mg/kg once daily. [1]
Kinase Assay	MEK1 enzymatic assays: NH2-terminal hexahistidine tagged, constitutively active MEK1 (S218D, S222D ΔR4F) is expressed in baculovirus-infected Hi5 insect cells and purified by immobilized metal affinity chromatography, ion exchange, and gel filtration. The activity of MEK1 is assessed by measuring the incorporation of [γ- 33P]phosphate from [γ-33P]ATP onto ERK2. The assay is carried out in a 96-well polypropylene plate with an incubation mixture (100 μL) composed of 25 mM HEPES (pH 7.4), 10 mM MgCl2, 5 mM β-glycerolphosphate, 100 μM sodium orthovanadate, 5 mM DTT, 5 nM MEK1, 1 μM ERK2, and 0 to 80 nM AZD8330 (final concentration of 1% DMSO). The reactions are initiated by the addition of 10 μM ATP (with 0.5 μC k[γ-33P]ATP/well) and incubated at room temperature for 45 min. An equal volume of 25% trichloracetic acid is added to stop the reaction and precipitate the proteins. Precipitated proteins are trapped onto glass fiber B filter plates, excess labeled ATP is washed off with 0.5% phosphoric acid, and radioactivity is counted in a liquid scintillation counter. ATP dependence is determined by varying the amount of ATP in the reaction mixture. The data are globally fitted.
Cell Research	Malme-3M melanoma cells are plated in 96-wells and treated with various concentrations of AZD8330 for 1 hour at 37 °C. The cells are fixed, permeabilized, and incubated with an anti-phospho-ERK antibody and an anti-ERK 1/2 antibody. Plates are washed and fluorescently-labeled secondary antibodies are added. Plates are analyzed on a LICOR fluorescence imager. The pERK signal is normalized to the total ERK signa (Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 85 mg/mL (184.29 mM),Sonication is recommended. DMSO: 85 mg/mL (184.29 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1681 mL	10.8406 mL	21.6812 mL
5 mM	0.4336 mL	2.1681 mL	4.3362 mL
10 mM	0.2168 mL	1.0841 mL	2.1681 mL
50 mM	0.0434 mL	0.2168 mL	0.4336 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.

Reference

Wallace EM, et al. AACR Annual Meeting, 2009, Abst 3696.
Yang Y, Suo N, Cui S, et al.Trametinib, an anti-tumor drug, promotes oligodendrocytes generation and myelin formation.Acta Pharmacologica Sinica.2024: 1-13.
Yeh TC, et al. Clin Cancer Res, 2007, 13(5), 1576-1583.