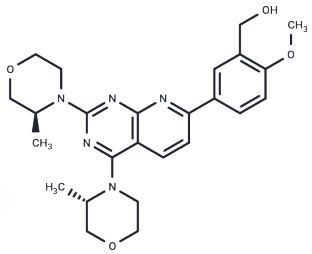
Data Sheet (Cat.No.T1859)

TargetMol

AZD-8055

Chemical Properties



CAS No. : 1009298-09-2

Formula: C25H31N5O4

Molecular Weight: 465.54

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	AZD-8055 is an orally bioavailable, highly selective, ATP-competitive mTOR kinase inhibitor that directly binds to the ATP-binding pocket of the mTOR kinase domain, while potently inhibiting both mTORC1 and mTORC2 complexes (IC_{50} values of 0.8 nM and 0.1 nM, respectively). AZD-8055 is suitable for research in oncology, metabolic diseases, and fibrotic disorders.
Targets(IC50)	Apoptosis,Autophagy,mTOR
In vitro	**Methods**: HPCAL1 was knocked down in Huh7 human hepatocellular carcinoma cells using shRNA. Following transfection, cells were treated with AZD-8055 at gradient concentrations (0, 10, 50, 100, 500 nM) for 72 hours. Cell viability was assessed using the CCK-8 assay. **Results**: HPCAL1-knockdown cells exhibited increased sensitivity to AZD-8055 (lower cell viability).[1] **Methods**: Uveal melanoma cell lines: 92.1, Mel202, MP38, MP41. AZD-8055 (1 μM) and romidepsin (25 ng/mL) were added. After 6 hours of romidepsin treatment, fresh medium was replaced, and cells were cultured for an additional 48 hours. Apoptosis was assessed by flow cytometry (Annexin V/SYTOX Green staining). **Results**: The combination of AZD-8055 and romidepsin induced the highest level of apoptosis in all four cell lines, outperforming other combinations. [2]
In vivo	**Methods**: A MYC/Trp53$^{-/-}$ liver cancer model was established via hydrodynamic tail-vein injection. Hpcal1 was simultaneously knocked out using CRISPR/Cas9 (sgHpcal1) or a control (sgCON). Following successful model establishment, AZD-8055 (10 mg/kg/day, once daily) was administered via intraperitoneal injection for 30 consecutive days. **Results**: AZD-8055 treatment significantly reduced tumor burden in sgHpcal1 mice, demonstrating superior efficacy compared to the sgCON group. [1]
Kinase Assay	The activity of mTOR was assayed using the recombinant mTOR technique described above. For inhibition experiments, AZD8055 was added to the reaction mixture and preincubated for 10 min before addition of ATP. Inhibition was performed at 1 to 3,000 nmol/L of AZD8055 in varying concentrations of ATP (40-200 μmol/L) [1].
Cell Research	For growth inhibition and acridine staining, cells were exposed to increasing concentrations of AZD8055 for 72 to 96 h and stained for cell nuclei (0.03 mg/mL Hoechst 33342) and acidic vesicles (1 μg/mL acridine orange). Images were captured at 450 and 536 nm on an ArrayScan II platform, and the percentage of acidic vesicles and

Cell Research	the number of cells were quantified. For LC3 assessment, cells were exposed to e64d/pepstatin (10 μg/mL) for 30 to 90 min before incubation with AZD8055. Cells were lysed on ice and analyzed by immunoblotting [1].
Animal Research	Tumor cells (10^6 for U87-MG, 5 × 10^6 for A549) were injected s.c. in a volume of 0.1 mL, and mice were randomized into control and treatment groups when tumor size reached 0.2 cm^3. AZD8055 was formulated in 30% (w/v) captisol (pH 3.0). The control group received the vehicle only. Tumor volumes (measured by caliper), animal body weight, and tumor condition were recorded twice weekly for the duration of the study. The tumor volume was calculated (taking length to be the longest diameter across the tumor and width to be the corresponding perpendicular diameter) using the following formula: (length × width) × √(length × width) × (π/6) [1].

Solubility Information

Solubility	Ethanol: 3 mg/mL (6.44 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 91 mg/mL (195.47 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: 4.5 mg/mL (9.67 mM),Solution. *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	2.148 mL	10.7402 mL	21.4804 mL
5 mM	0.4296 mL	2.148 mL	4.2961 mL
10 mM	0.2148 mL	1.074 mL	2.148 mL
50 mM	0.043 mL	0.2148 mL	0.4296 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

Chen T, et al. Hippocalcin-Like 1 blunts liver lipid metabolism to suppress tumorigenesis via directly targeting RUVBL1-mTOR signaling. Theranostics. 2022 Oct 24;12(17):7450-7464.
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Patel RP, et al. Dual Inhibition of Histone Deacetylases and the Mechanistic Target of Rapamycin Promotes Apoptosis in Cell Line Models of Uveal Melanoma. Invest Ophthalmol Vis Sci. 2021 Sep 2;62(12):16.
Xia Y, Chen J, Yu Y, et al. Compensatory combination of mTOR and TrxR inhibitors to cause oxidative stress and regression of tumors. Theranostics. 2021, 11(9): 4335.
You W, et al. Inhibition of mammalian target of rapamycin attenuates early brain injury through modulating microglial polarization after experimental subarachnoid hemorrhage in rats. J Neurol Sci. 2016 Aug 15;367:224-31.
Zhang W, Li X, Jiang M, et al.SOCS3 deficiency-dependent autophagy repression promote the survival of early-stage myeloid-derived suppressor cells in breast cancer by activating the Wnt/mTOR pathway.Journal of Leukocyte Biology.2023: qiad020.
Chen F, Peng S, Li C, et al.Nitidine chloride inhibits mTORC1 signaling through ATF4-mediated Sestrin2 induction and targets IGF2R for lysosomal degradation.Life Sciences.2024: 122918.
Wang Z, Feng J, Yu J, et al. FKBP12 mediates necroptosis by initiating RIPK1-RIPK3-MLKL signal transduction in response to TNF receptor 1 ligation[J]. Journal of cell science. 2019 May 20;132(10). pii: jcs227777.
Xia Y, Chen J, Yu Y, et al. Compensatory combination of mTOR and TrxR inhibitors to cause oxidative stress and regression of tumors[J]. Theranostics. 2021, 11(9): 4335.

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