

Product Data Sheet

Product Name: AZD8055

Cat. No.: GC16380

Chemical Properties

Cas. No. 1009298-09-2

Chemical Name [5-[2,4-bis[(3S)-3-methylmorpholin-4-yl]pyrido[2,3-d]pyrimidin-7-yl]-2-methoxyphenyl]methanol

SMILES CC1COCCN1C2=NC(=NC3=C2C=CC(=N3)C4=CC(=C(C=C4)OC)CO)N5CCOCC5C

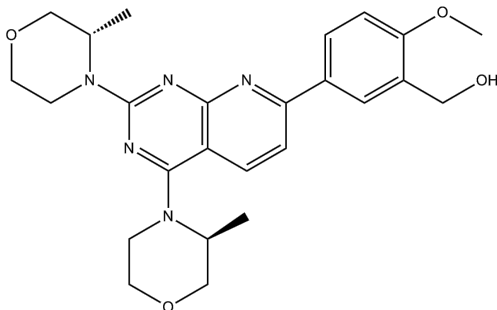
Formula $C_{25}H_{31}N_5O_4$ M.Wt 465.54

Solubility $\geq 23.3\text{mg/mL}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines

NB cell lines

Caution: Product has not been fully validated for medical applications. For research use only.

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Preparation method	Indicated cell lines were incubated in RPMI1640 + 10% FBS with/without AZD8055 (0.1 and 1µM) for 24h. Phosphorylation of mTOR signaling was detected by western blot.
Reaction Conditions	0.1 and 1uM; 24 h
Applications	AZD8055 inhibited both mTOR S2448 and mTOR S2481 phosphorylation significantly in a concentration dependent manner.
Animal experiment [2]:	
Animal models	C57BL/6 mice
Preparation method	After an overnight fast, mice were intraperitoneal (IP)-injected with vehicle or AZD8055 (10 mg/kg). 3h after AZD8055 injection additional blood was sampled for plasma insulin and fatty acids (FA) determinations.
Dosage form	10 mg/kg; i.p.
Applications	long with elevated glucose levels at 3h, AZD8055 treated mice had 3-fold higher plasma insulin levels and lower plasma FAs.

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References:

[1] Xu D Q , Toyoda H , Yuan X J , et al. Anti-tumor effect of AZD8055 against neuroblastoma cells in vitro and in vivo[J]. Experimental Cell Research, 2018, 365(2).

[2] Kleinert M, Sylow L, Fazakerley D J, et al. Acute mTOR inhibition induces insulin resistance and alters substrate utilization in vivo[J]. Molecular metabolism, 2014, 3(6): 630-641.

Background

AZD8055 is a new ATP-competitive mTOR inhibitor with an IC_{50} of 0.8 nmol/L and a K_i of 1.3 nmol/L^[1]. mTOR is a serine/threonine kinase, and AZD8055 is a potent mTORC1/mTORC2 dual inhibitor^[2]. AZD8055 significantly inhibits the phosphorylation of Akt^{Ser473} and induces apoptosis^[3].

In vitro, AZD8055 (5 nmol/L) resulted in 70% to 80% inhibition of p70S6K in MCF-7 and HEK cells. AZD8055 also inhibited a variety of cancer cells (including U87MG, BT474c, A549, Calu-3, LoVo, SW620 , PC3 and MES-SA, etc.) show obvious anti-cancer activity^[1]. AZD8055 (0.1 and 1μM) significantly inhibits the activity of mTORC1 and mTORC2, thereby inhibiting Akt^{Ser473} phosphorylation in human neuroblastoma cell lines, and also inhibits cell growth in vitro by inducing autophagy, apoptosis and cell cycle arrest^[2]. The IC_{50} of AZD8055 against several laryngeal cancer cell lines are: UM-SCC-98 (~40μM), UM-SCC-12 (~23μM), and UM-SCC-11A (~8μM)^[4].

In vivo, AZD8055 (5 mg/kg) was injected intraperitoneally every other day for xenograft model mice for eight times in total, which inhibited tumor growth and had no obvious adverse effects on the body weight of the mice^[2]. Intraperitoneal injection of AZD8055 (10 mg/kg) into mice transiently increases plasma insulin levels 3-fold, induces insulin resistance in mice, and impairs mTOR signaling in insulin-responsive tissues. It also causes increased lipid oxidation and glucose Intolerance^[5]. Oral treatment of PTEN^{+/-}-LKB1^{+/-}hypo mice with AZD8055 (20mg/kg) for 42 days induced a reduction of approximately 40% in tumor volume and simultaneously ablated the phosphorylation of AKT, S6K and SGK protein kinases^[6].

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- [1] Chresta CM, et al. AZD8055 is a potent, selective, and orally bioavailable ATP-competitive mammalian target of rapamycin kinase inhibitor with in vitro and in vivo antitumor activity. *Cancer Res*, 2010, 70(1), 288-298.
- [2] Xu D Q , Toyoda H , Yuan X J ,et al. Anti-tumor effect of AZD8055 against neuroblastoma cells in vitro and in vivo[J]. *Experimental Cell Research*, 2018, 365(2).
- [3] Kawata T, Tada K, Kobayashi M, et al. Dual inhibition of the mTORC 1 and mTORC 2 signaling pathways is a promising therapeutic target for adult T-cell leukemia[J]. *Cancer science*, 2018, 109(1): 103-111.
- [4] Gobin C, Chang M, Lattimore C C, et al. Exploring the association between miR-9-5p levels and the mTORC1/mTORC2 pathway in laryngeal cancer cell lines[J]. *Cancer Research*, 2024, 84(6_Supplement): 5696-5696.
- [5] Kleinert M, Sylow L, Fazakerley D J, et al. Acute mTOR inhibition induces insulin resistance and alters substrate utilization in vivo[J]. *Molecular metabolism*, 2014, 3(6): 630-641.
- [6] Garcia-Martinez J M, Wullschleger S, Preston G, et al. Effect of PI3K-and mTOR-specific inhibitors on spontaneous B-cell follicular lymphomas in PTEN/LKB1-deficient mice[J]. *British journal of cancer*, 2011, 104(7): 1116-1125.

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