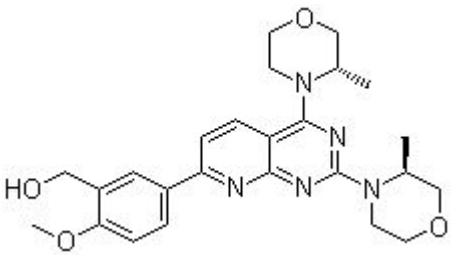
Product Introduction

AZD8055

AZD8055 is a novel ATP-competitive **mTOR** inhibitor with **IC50** of 0.8 nM with excellent selectivity (～1,000-fold) against PI3K isoforms and ATM/DNA-PK. Phase 1.

Technical Data:

Molecular Weight (MW):	465.54	
Formula:	$C_{25}H_{31}N_5O_4$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 93 mg/mL	
	Water <1 mg/mL	
	Ethanol 3 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	1009298-09-2	

Biological Activity

AZD8055 shows low activity (～1,000-fold) against all PI3K isoforms (α, β, γ, δ) and other members of the PI3K-like kinase family (ATM and DNA-PK). AZD8055 inhibits the phosphorylation of mTORC1 (p70S6K and 4E-BP1) as well as phosphorylation of the mTORC2 (Akt) and downstream proteins. The rapamycin-resistant T37/46 phosphorylation sites on 4E-BP1 can be fully inhibited by AZD8055, resulting in significant inhibition of cap-dependent translation. AZD8055 potently inhibits proliferation in U87MG, A549 and H838 cells with IC50 of 53, 50 and 20 nM, respectively. AZD8055 also induces autophagy and

increased LC3-II levels in H838 and A549 cells. [1] AZD8055 decreases AML blast cell proliferation and cell cycle progression, reduces the clonogenic growth of leukemic progenitors and induces caspase-dependent apoptosis in leukemic cells but not in normal immature CD34+ cells. [2] AZD8055 indicates inhibitory against the pediatric preclinical testing program (PPTP) cell lines with IC50 of 24.7 nM and induces significant differences in EFS distribution. [3]

AZD8055 inhibits the pS6 and pAkt in U87MG and A549 xenografts at 2.5/10 mg/kg, which leads to tumor growth inhibition. AZD8055 shows significant antitumor activity in many xenografts, including U87MG, BT474c, A549, Calu-3, LoVo, SW620, PC3 and MES-SA at a dose of 10/20 mg/kg. [1] AZD8055 induces ~40% reduction in tumour volume, accompanied by ablation of phosphorylation of Akt, S6K and SGK protein kinases. Administration of AZD8055 (5mg/kg, Bid) and SAHA (100 mg/kg/d) results in complete tumor growth inhibition in PTEN+/−LKB1+/hypo xenografts without side effects on mice by inhibition of mTORC1 and mTORC2 signaling. [4]

First drug to inhibit both types of mTOR protein.

References

[1] Chresta CM, et al. Cancer Res, 2010, 70(1), 288-298.

[2] Willems L, et al. Leukemia, 2011, doi: 10.1038/leu.2011.339.

[3] Houghton PJ, et al. Pediatr Blood Cancer, 2012, 58(2), 191-199.

[4] García-Martínez JM, et al. Br J Cancer, 2011, 104(7), 1116-1

Note： Products protected by valid patents are not offered for sale in countries where the sale of such products constitutes a patent infringement and its liability is at buyer’s risk. This item is only for R&D purpose not for commercial business in kilos. Buyers should overview the patent issue in their countries.