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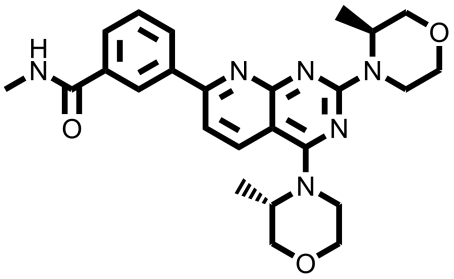
mTOR Inhibitor – AZD2014

Chemical Name: 3-(2,4-bis((S)-3-methylmorpholino)pyrido[2,3-d]pyrimidin-7-yl)-N-methylbenzamide



Molecular Weight:	462.54
Formula:	$C_{25}H_{30}N_6O_3$
Purity:	≥ 98%
CAS#:	1009298-59-2
Solubility:	DMSO up to 100 mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

Biological Activity:

AZD2014 is a highly potent, selective and ATP-competitive mTOR inhibitor (IC_{50} = 2.8 nM). It displays a high level of selectivity against other members of the PIKK family (IC_{50} against PI3K isoforms α, β, γ, δ = 3.8 μM, >30 μM, >30 μM and >29 μM, respectively) and is inactive against a general panel of over 200 kinases when tested at 10 μM. AZD2014 inhibits both mTORC1 and mTORC2 in vitro (pS6 ($S^{235/236}$) IC_{50} = 0.2 μM, pAKT (S^{473}) IC_{50} = 0.08 μM) and has shown dose-dependent tumor growth inhibition in a mouse MCF7 xenograft model alongside modulation of mTORC1 and mTORC2 biomarkers. Different from AZD8055, AZD2014 shows consistent exposure in rodents and a low turnover in human hepatocyte incubations. It is in phase I clinical development for advanced solid malignancies.

How to Use:

In vitro: AZD2014 was used at 2.5-5 μM concentration in vitro and cellular assays.

In vivo: AZD2014 was orally dosed to mice at 2.5-20 mg/kg once or twice per day to inhibit tumor growth.

Reference:

1. Guichard SM, at al. AZD2014, a dual mTORC1 and mTORC2 inhibitor is differentiated from allosteric inhibitors of mTORC1 in ER+ breast cancer. (2012) AACR Annual Meeting: Chicago, Abstract 917.
2. Pike KG, et al. Optimization of potent and selective dual mTORC1 and mTORC2 inhibitors: The discovery of AZD8055 and AZD2014. (2013) Bioorg Med Chem Lett. In press.