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Data Sheet

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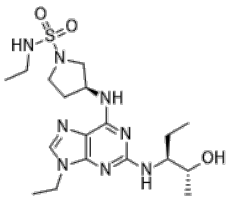
Product Name	:	AZD8421
Cat. No.	:	PC-22118
CAS No.	:	3047321-53-6
Molecular Formula	:	$C_{18}H_{32}N_8O_3S$
Molecular Weight	:	440.57
Target	:	Cyclin-dependent Kinase (CDK)
Solubility	:	10 mM in DMSO



Biological Activity

AZD8421 (AZD-8421) is a potent, highly selective **CDK2 i**nhibitor with IC50 of 9 nM, >300-fold selectivity over CDK9.
AZD8421 forms hydrogen bonding interaction with Lys89 (a CDK2-specific residue) near the solvent region of the ATP-binding pocket.
AZD8421 displays high selectivity over CDK1, CDK4 and CDK6.
AZD8421 potently inhibits cell proliferation (69 nM, OVCAR3), correlated with inhibition of pRB, arrest in G1/S phase of the cell cycle and induction of senescence, in a CCNE1 amplified cell line.
AZD8421 shows combination benefit when combined with approved CDK4/6 inhibitors in CDK4/6 inhibitor resistant breast cancer cell lines.
AZD8421 potently suppresses phosphorylation of Rb, and demonstrates robust monotherapy and CDK4/6i combination activity in breast and ovarian in vivo models.
AZD8421 shows robust monotherapy activity in a CCNE1 amplified ovarian model OVCAR3 with regressions seen with monotherapy and in combination with palbociclib in CDK4/6 inhibitor resistant breast PDXs.

References

Christopher R. Denz, et al. ***Cancer Res*** (2024) 84 (7_Supplement): ND06.

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