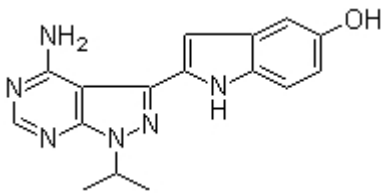
Product Introduction

PP242

PP242 is a selective **mTOR** inhibitor with **IC50** of 8 nM; targets both mTOR complexes with >10- and 100-fold selectivity for mTOR than PI3Kδ or PI3Kα/β/γ, respectively.

Technical Data:

Molecular Weight (MW):	308.34	
Formula:	$C_{16}H_{16}N_6O$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 62 mg/mL	
	Water <1 mg/mL	
	Ethanol 18 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	1092351-67-1	

Biological Activity

PP242 exhibits potent selectivity for mTOR over other PI3K family kinases such as p110α, p110β, p110γ, p110δ, and DNA-PK with IC50 of 1.96 μM, 2.2 μM, 1.27 μM, 0.102 μM, and 0.408 μM, respectively. PP242 displays some inhibitory activity against Ret, PKCα, PKCβ, and JAK2, while exhibits remarkable selectivity against 215 other protein kinases. Unlike rapamycin, PP242 inhibits both mTORC1 and mTORC2. In BT549 cells, PP242 treatment (0.04-10 μM) inhibits the phosphorylation of Akt, the mTOR substrate p70S6K, and its downstream target S6 in a dose-dependent manner. [1] PP242 potently inhibits PKCα with IC50 of 49

nM. Low concentrations of PP242 inhibit the phosphorylation of Akt S473 and higher concentrations partially inhibit Akt T308-P in addition to S473-P. As PP242 is a more effective mTORC1 inhibitor than rapamycin, PP242 inhibits the proliferation of primary MEFs, and the phosphorylation of 4EBP1 at T36/45 and S65, more potently than rapamycin. PP242 but not rapamycin potently inhibits cap-dependent translation, by causing a higher level of binding between 4EBP1 and eIF4E than rapamycin. [2] PP242 potently inhibits the proliferation of p190-transformed murine BM, SUP-B15, and K562 cells with GI50 of 12 nM, 90 nM, and 85 nM, respectively. PP242 also inhibits the growth of solid tumor cell lines such as SKOV3, PC3, 786-O, and U87 with GI50 of 0.49 μM, 0.19 μM, 2.13 μM, and 1.57 μM, respectively. [3] PP242 is also more effective than rapamycin in achieving cytoreduction and apoptosis in multiple myeloma (MM) cells. [4

Administration of PP242 is able to completely inhibit the phosphorylation of Akt at S473 and T308 in fat and liver of mice. PP242 only partially inhibits the phosphorylation of Akt in skeletal muscle and is more effective at inhibiting the phosphorylation of T308 than S473, despite able to fully inhibit the phosphorylation of 4EBP1 and S6. [2] Oral administration PP242 potently delays the leukemia onset in the mice model, and induces leukemia regression by inhibiting mTORC2 and mTORC1 activation that correlates with loss in cell size. [3] PP242 treatment potently inhibits the growth of 8226 cells in mice. [4] One of the first selective inhibitors that targets ATP domain of mTOR.

References

[1] Apsel B, et al. Nat Chem Biol, 2008, 4(11), 691-699.

[2] Feldman ME, et al. PLoS Biol, 2009, 7(2), 0371-0383.

[3] Janes MR, et al. Nat Med, 2010, 16(2), 205-213.

[4] Hoang B, et al. Blood, 2010, 116(22), 4560-4568.

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