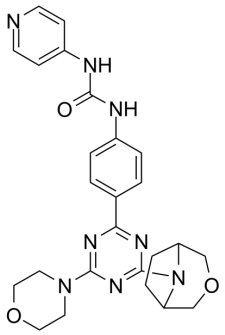
PKI-179

Cat. No.:	HY-11080
CAS No.:	1197160-28-3
Molecular Formula:	$C_{25}H_{28}N_8O_3$
Molecular Weight:	488.54
Target:	PI3K; mTOR
Pathway:	PI3K/Akt/mTOR
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



BIOLOGICAL ACTIVITY

Description

PKI-179 is a potent and orally active dual PI3K/mTOR inhibitor, with IC_{50}s of 8 nM, 24 nM, 74 nM, 77 nM, and 0.42 nM for PI3K-α, PI3K-β, PI3K-γ, PI3K-δ and mTOR, respectively. PKI-179 also exhibits activity over E545K and H1047R, with IC_{50}s of 14 nM and 11 nM, respectively. PKI-179 shows anti-tumor activity in vivo[1][2].

IC_{50} & Target

mTOR 0.42 nM (IC_{50})	PI3Kα 8 nM (IC_{50})	PI3Kβ 24 nM (IC_{50})	PI3Kγ 74 nM (IC_{50})
PI3Kδ 77 nM (IC_{50})	E545K 14 nM (IC_{50})	H1047R 11 nM (IC_{50})	

In Vitro

PKI-179 inhibits the cell proliferation, with IC_{50}s of 22 nM and 29 nM for MDA361 and PC3 cells, respectively[1].
PKI-179 shows inhibitory activity against a panel of 361 other kinases, hERG and cytochrome P450 (CYP) isoforms at concentrations up to >30 μM, but does have activity for CYP2C8 (IC_{50}=3 μM)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

PKI-179 (5-50 mg/kg; p.o. once daily for 40 days) inhibits the tumor growth and is well tolerated in nude mice bearing MDA-361 human breast cancer tumors[1].
PKI-179 (50 mg/kg; p.o.) results in good inhibition of PI3K signaling in nude mice bearing MDA361 tumor xenografts[1].
PKI-179 exhibits good oral bioavailability (98% in nude mouse, 46% in rat, 38% in monkey, and 61% in dog) and a high half-life (>60 min) [1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Nude mice bearing MDA-361 human breast cancer tumors[1]
Dosage:	5, 10, 25, 50 mg/kg
Administration:	I.p. every 3 days for 4 weeks
Result:	Exhibited pronounced tumor growth arrest when dosed above 10 mg/kg. No significant weight loss of tested animals was observed for all different dosages.

REFERENCES

[1]. Venkatesan AM, et, al. PKI-179: an orally efficacious dual phosphatidylinositol-3-kinase (PI3K)/mammalian target of rapamycin (mTOR) inhibitor. Bioorg Med Chem Lett. 2010 Oct 1;20(19):5869-73.

[2]. Rehan M. A structural insight into the inhibitory mechanism of an orally active PI3K/mTOR dual inhibitor, PKI-179 using computational approaches. J Mol Graph Model. 2015 Nov;62:226-234.

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