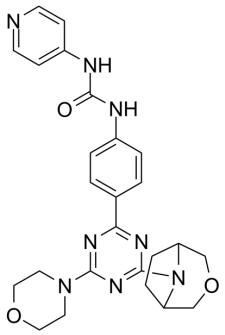
PKI-179

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (204.69 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0469 mL	10.2346 mL	20.4692 mL
	5 mM	0.4094 mL	2.0469 mL	4.0938 mL
	10 mM	0.2047 mL	1.0235 mL	2.0469 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.12 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.12 mM); Clear solution

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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