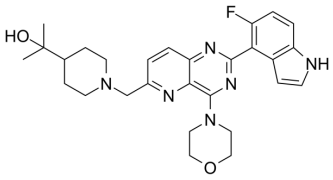
PI3kδ inhibitor 1

Cat. No.:	HY-15288
CAS No.:	1332075-63-4
Molecular Formula:	$C_{28}H_{33}FN_6O_2$
Molecular Weight:	504.6
Target:	PI3K
Pathway:	PI3K/Akt/mTOR
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	PI3kδ inhibitor 1 is a potent and selective PI3Kδ inhibitor with an IC_{50} of 3.8 nM.
IC_{50} & Target	PI3Kδ 3.8 nM (IC_{50})
In Vitro	PI3kδ inhibitor 1 (Compound 3) is a potent inhibitor of PI3Kδ that is 200-400 fold selective for all three remaining Class I PI3K isoforms and extremely selective relative to 239 kinases tested in SelectScreen service (0/239 kinases showing >50% inhibition when tested at 1 μM; mTOR, DNA-PK, VPS34, PI4Kα and PI4Kβ are inhibited at 10% or less when tested at 1 μM; PIKC2A and PIKC2B are inhibited at 11% and 42%, respectively, at this same concentration and show less than 10% inhibition when tested at 0.1 μM; the PIKK family kinases ATM and ATR are not assessed)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The pharmacokinetic properties of PI3kδ inhibitor 1 (Compound 3) are evaluated in mice and rats when dosed IV and orally. Good plasma exposures and reasonable half-lives are observed upon oral dosing, a reflection of high oral bioavailability (80% and 90% at a low dose for mouse and rat, respectively), moderate volume of distribution, and moderate clearance. PI3kδ inhibitor 1 has moderate terminal elimination half-life ($t_{1/2}$=2.6 h, 2.9 h, 5 h, 2.6, 3.8 and 4.8 h for mouse (5 mg/kg, po), mouse (20 mg/kg, po), mouse (40 mg/kg, po), rat (5 mg/kg, po), rat (10 mg/kg, po), rat (30 mg/kg, po)). Plasma exposures and Cmax levels increase with dose in both mice and rats, important in that inflammatory disease models utilize these two species. Plasma protein binding for PI3kδ inhibitor 1 ranges from 80-88% in rodents and is consistent with values obtained in human plasma (86%)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice and Rats[1] Female mice are dosed IV (intravenously) with PI3kδ inhibitor 1 in 5% DMSO/5% Cremephor and PO (orally) as an MCT suspension (0.5% methylcellulose/0.2% Tween-80). The IV (1 mg/kg) and PO (5, 20 and 40 mg/kg) studies are performed in CD-1 mice while the higher dose studies are performed in the Balb/c strain. Male Sprague-Dawley rats are dosed with the same IV (1 mg/kg) and PO (5, 10 and 30 mg/kg) formulations as those used for mice. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Sutherlin DP, et al. Potent and selective inhibitors of PI3Kδ: obtaining isoform selectivity from the affinity pocket and tryptophan shelf. Bioorg Med Chem Lett. 2012 Jul 1;22(13):4296-302.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA