
Product Data Sheet

Product Name: PI3k δ inhibitor 1

Cat. No.: GC36911

Chemical Properties

Cas. No. 1332075-63-4

SMILES CC(O)(C1CCN(CC2=NC3=C(N4CCOCC4)N=C(C5=C(F)C=CC6=C5C=CN6)N=C3C=C2)CC1)CFormula $C_{28}H_{33}FN_6O_2$ M.Wt 504.6

Solubility Soluble in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure **Protocol****Animal experiment:**

Mice and Rats[1]Female mice are dosed IV (intravenously) with PI3k δ 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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References:

[1]. Sutherlin DP, et al.
Potent and selective
inhibitors of PI3K δ :
obtaining isoform
selectivity from the affinity
pocket and tryptophan
shelf. Bioorg Med Chem
Lett. 2012 Jul
1;22(13):4296-302.

Background

PI3k δ inhibitor 1 is a potent and selective PI3K δ inhibitor with an IC₅₀ of 3.8 nM. PI3K δ |3.8 nM (IC₅₀)

PI3k δ inhibitor 1 (Compound 3) is a potent inhibitor of PI3K δ 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 μ M; mTOR, DNA-PK, VPS34, PI4K α and PI4K β are inhibited at 10% or less when tested at 1 μ M; 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 μ M; the PIKK family kinases ATM and ATR are not assessed)[1].

The pharmacokinetic properties of PI3k δ 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. PI3k δ 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 C_{max} levels increase with dose in both mice and rats, important in that inflammatory disease models utilize these two species. Plasma protein binding for PI3k δ inhibitor 1 ranges from 80-88% in rodents and is consistent with values obtained in human plasma (86%)[1].

[1]. Sutherlin DP, et al. Potent and selective inhibitors of PI3K δ : obtaining isoform selectivity from the affinity pocket and tryptophan shelf. Bioorg Med Chem Lett. 2012 Jul 1;22(13):4296-302.

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