Web: www.taiclone.com
Tel: +886-2-2735-9682
Email: order@taiclone.com

PIK-75

Catalog No: tcsc0505

Available Sizes

Size: 10mg

Size: 50mg

Size: 100mg

Specifications

CAS No:
372196-77-5

Formula:
$C_{16}H_{15}BrClN_5O_4S$

Pathway:
PI3K/Akt/mTOR;Cell Cycle/DNA Damage;PI3K/Akt/mTOR

Target:
DNA-PK;DNA-PK;PI3K

Purity / Grade:
>98%

Solubility:
DMSO : ≥ 30 mg/mL (61.38 mM)

Alternative Names:
PIK-75 Hydrochloride

Observed Molecular Weight:
488.74

Product Description

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PIK-75 is a **DNA-PK** and **PI3K** inhibitor, which inhibits DNA-PK, **p110α** and p110γ with **IC_{50}**s of 2, 5.8 and 76 nM, respectively. PIK-75 inhibits p110α >200-fold more potently than p110β (IC_{50}=1.3 μM).

IC50 & Target: IC50: 2 nM (DNA-PK), 5.8 nM (p110α), 76 nM (p110γ), 510 nM (p110δ), ~1 μM (PI3KC2β), ~1 μM (mTORC1), 1.3 μM (p110β), 2.3 μM (ATM), 2.6 μM (hsVPS34), ~10 μM (PI3KC2α), ~10 μM (mTORC2), ~50 μM (PI4KIIIβ), 21 μM (ATR)[1]

In Vitro: PIK-75 also inhibits p110δ, PI3KC2β, mTORC1, ATM, hsVPS34, PI3KC2α, mTORC2, ATR and PI4KIIIβ with IC_{50}s of 510 nM, ~1 μM, ~1 μM, 2.3 μM, 2.6 μM, ~10 μM, ~10 μM, 21 μM, ~50 μM, respectively. PIK-75 alone blocks Thr 308 phosphorylation in L6 myotubes and 3T3-L1 adipocytes with IC_{50} values of 1.2 and 1.3 μM, respectively[1]. PIK-75 is a competitive p110α inhibitor with respect to a substrate, phosphatidylinositol (PI) in contrast to most other PI3K inhibitors, which bind at or near the ATP site. Using sequence analysis and the existing crystal structures of inhibitor complexes with the p110γ and p110δ isoforms, a new region of nonconserved amino acids (region 2) is identified that is postulated to be involved in PIK-75 p110α selectivity. Analysis of region 2, using in vitro mutation of identified nonconserved amino acids to alanine, shows that Ser773 is a critical amino acid involved in PIK-75 binding, with an 8-fold-increase in the IC_{50} compared with wild-type. Further kinetic experiments are undertaken to determine the effect of PIK-75 on the kinetics of binding of ATP and PI to the p11α S773D mutant. Activity is estimated using a range of PI concentrations at the concentrations of 0, 50, 100 and 200 nM PIK-75. The K_m for PI is 11.2 μM compared with 7.0 μM for the wild-type enzyme. The K_i for PIK-75 is estimated to be 146 nM, a 64-fold increase on the value estimated for the wild-type enzyme (2.3 nM)[2]. MIA PaCa-2 and AsPC-1 cells are treated with increasing concentration of PIK-75 for 48 h and the cell viability is determined by MTT assay. PIK-75 inhibits the proliferation of pancreatic cancer cells via apoptotic cell death. Submicromolar concentration of PIK-75 is sufficient to inhibit the proliferation of pancreatic cancer, MIA PaCa-2 and AsPC-1 cells after 48-h treatment. PIK-75 also reduces the colony formation of pancreatic cancer MIA PaCa-2 and AsPC-1 cells[3]

In Vivo: PIK-75 enhances the antitumor effect of Gemcitabine in vivo. The effect of PIK-75/Gemcitabine combination is further demonstrated by in vivo mouse xenograft model. Mice bearing tumors of MIA PaCa-2 are administered with Gemcitabine (20 mg/kg), PIK-75 (2 mg/kg), or combination of both drugs. Since PIK-75 is a reversible inhibitor, PIK-75 is administered 5 times per week to ensure maintaining sufficient inhibitory effects. Gemcitabine is administered twice per week. Gemcitabine or PIK-75 reduces the tumor growth to similar degree[3]