

# 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 :  $\geq 30$  mg/mL (61.38 mM)

**Alternative Names:**

PIK-75 Hydrochloride

**Observed Molecular Weight:**

488.74

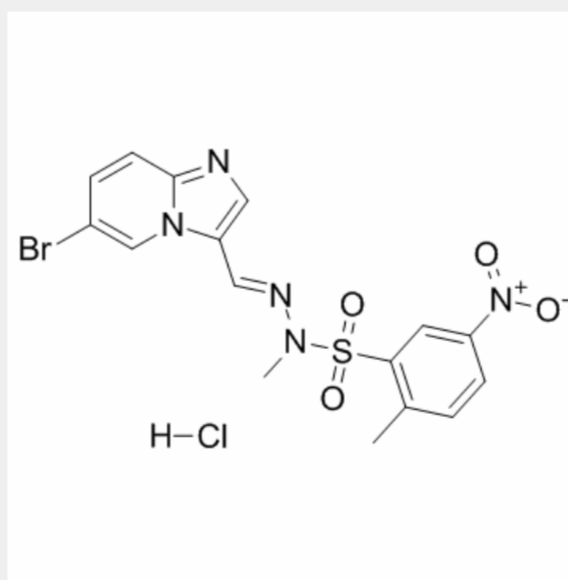
## Product Description

PIK-75 is a **DNA-PK** and **PI3K** inhibitor, which inhibits DNA-PK, **p110 $\alpha$**  and p110 $\gamma$  with **IC<sub>50</sub>**s of 2, 5.8 and 76 nM, respectively. PIK-75 inhibits p110 $\alpha$  >200-fold more potently than p110 $\beta$  (IC<sub>50</sub>=1.3  $\mu$ M).

IC50 & Target: IC50: 2 nM (DNA-PK), 5.8 nM (p110 $\alpha$ ), 76 nM (p110 $\gamma$ ), 510 nM (p110 $\delta$ ), ~1  $\mu$ M (PI3KC2 $\beta$ ), ~1  $\mu$ M (mTORC1), 1.3  $\mu$ M (p110 $\beta$ ), 2.3  $\mu$ M (ATM), 2.6  $\mu$ M (hsVPS34), ~10  $\mu$ M (PI3KC2 $\alpha$ ), ~10  $\mu$ M (mTORC2), ~50  $\mu$ M (PI4KIII $\beta$ ), 21  $\mu$ M (ATR)<sup>[1]</sup>

**In Vitro:** PIK-75 also inhibits p110 $\delta$ , PI3KC2 $\beta$ , mTORC1, ATM, hsVPS34, PI3KC2 $\alpha$ , mTORC2, ATR and PI4KIII $\beta$  with IC<sub>50</sub>s of 510 nM, ~1  $\mu$ M, ~1  $\mu$ M, 2.3  $\mu$ M, 2.6  $\mu$ M, ~10  $\mu$ M, ~10  $\mu$ M, 21  $\mu$ M, ~50  $\mu$ M, respectively. PIK-75 alone blocks Thr 308 phosphorylation in L6 myotubes and 3T3-L1 adipocytes with IC<sub>50</sub> values of 1.2 and 1.3  $\mu$ M, respectively<sup>[1]</sup>. PIK-75 is a competitive p110 $\alpha$  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 p110 $\gamma$  and p110 $\delta$  isoforms, a new region of nonconserved amino acids (region 2) is identified that is postulated to be involved in PIK-75 p110 $\alpha$  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<sub>50</sub> 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 p11 $\alpha$  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<sub>m</sub> for PI is 11.2  $\mu$ M compared with 7.0  $\mu$ M for the wild-type enzyme. The K<sub>i</sub> 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)<sup>[2]</sup>. 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<sup>[3]</sup>

**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<sup>[3]</sup>



All products are for RESEARCH USE ONLY. Not for diagnostic & therapeutic purposes!