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

VS-5584

Catalog No: tcsc1202

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Specifications

CAS No:
1246560-33-7

Formula:
$C_{17}H_{22}N_8O$

Pathway:
PI3K/Akt/mTOR;PI3K/Akt/mTOR

Target:
PI3K;mTOR

Purity / Grade:
>98%

Solubility:
10 mM in DMSO

Alternative Names:
SB2343

Observed Molecular Weight:
354.41

Product Description

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VS-5584 is a **pan-PI3K/mTOR** kinase inhibitor with **IC_{50}**s of 16 nM, 68 nM, 42 nM, 25 nM, and 37 nM for PI3Kα, PI3Kβ, PI3Kδ, PI3Kγ and mTOR, respectively. VS-5584 simultaneously blocks **mTORC2** as well as **mTORC1**.

IC50 & Target: IC50: 16 nM (PI3Kα), 68 nM (PI3Kβ), 42 nM (PI3Kδ), 25 nM (PI3Kγ), 37 nM (mTOR)[1]

mTORC1, mTORC2[2]

In Vitro: VS-5584 is an ATP-competitive inhibitor which selectively inhibits PI3K/mTOR signaling with equivalent low nanomolar potency against all human Class I PI3K isoforms and mTOR kinase. VS-5584 (0.001, 0.01, 0.1,1,10 and 100 μM) preferentially inhibits cancer stem cells in HMLE breast cancer cells while Paclitaxel increases the percentage of cancer stem cells. VS-5584 (0.1, 1, 10, 100 and 1000 nM) reduces the number of Aldefluor-positive cancer stem cells while Paclitaxel increases the percentage of cancer stem cells. VS-5584 (10, 30, 100, 300 nM) reduces the percentage of cancer stem cells (side population) in a Hoechst dye exclusion assay[1]. VS-5584 is a potent inhibitor of mTOR (IC_{50}=37 nM) as well as class I PI3K isoforms (IC_{50}: PI3Kα=16 nM; PI3Kβ=68 nM; PI3Kγ=25 nM; PI3Kδ=42 nM). All other evaluated kinases show negligible binding when tested up to 10 μM VS-5584[1].

In Vivo: Nude mice bearing MDA-MB-231 human breast cancer tumors are treated for 5 days with once daily oral VS-5584 (25 mg/kg). Oral treatment of tumor bearing mice with VS-5584 reduces cancer atem cells analyzed from extracted tumors. Mice are implanted with tumor fragments from a docetaxel-resistant patient-derived triple negative breast cancer. Mice are treated with VS-5584 (20 mg/kg, po, qd) or Docetaxel (20 mg/kg, i.v.). Oral VS-5584 induces tumor regression in a Docetaxel-resistant patient-derived breast cancer model[1]. A single oral dose of VS-5584 is rapidly absorbed with a t_{max} of 0.9 hours and an elimination half-life of 10 hours. To determine the pharmacokinetic and pharmacodynamic relationship in tumors, PC3-tumor–bearing mice are treated with a single dose of VS-5584 and plasma and tumors are harvested after 6 hours and analyzed for concentrations of VS-5584 and effects on target efficacy biomarkers. Plasma levels of VS-5584 increase dose-dependently. For evaluation of efficacy in a Rapamycin-sensitive PC3 engraftment model, tumor-bearing mice are treated with VS-5584 for 28 days in comparison with the rapalog Everolimus. VS-5584 is well tolerated at both doses tested (11 and 25 mg/kg) with minimal weight loss (mean 4.7% on day 27). Treatment with VS-5584 leads to significant tumor growth inhibition (TGI) of 79% and 113% for 11 and 25 mg/kg, respectively[1].