

# 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

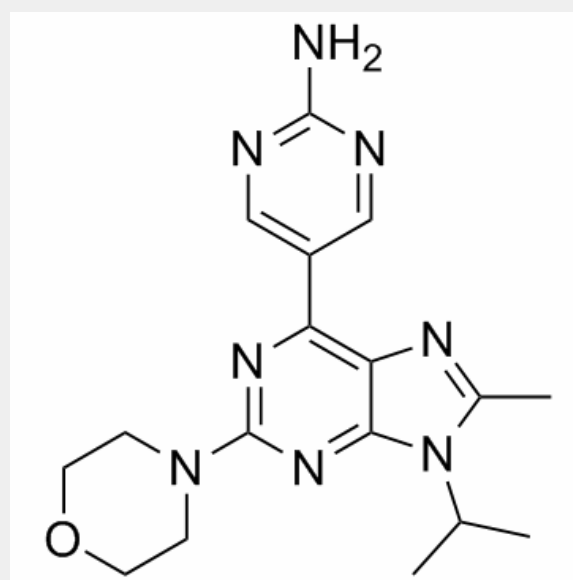
VS-5584 is a **pan-PI3K/mTOR** kinase inhibitor with **IC<sub>50</sub>**s of 16 nM, 68 nM, 42 nM, 25 nM, and 37 nM for PI3K $\alpha$ , PI3K $\beta$ , PI3K $\delta$ , PI3K $\gamma$  and mTOR, respectively. VS-5584 simultaneously blocks **mTORC2** as well as **mTORC1**.

IC50 & Target: IC50: 16 nM (PI3K $\alpha$ ), 68 nM (PI3K $\beta$ ), 42 nM (PI3K $\delta$ ), 25 nM (PI3K $\gamma$ ), 37 nM (mTOR)<sup>[1]</sup>

mTORC1, mTORC2<sup>[2]</sup>

**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  $\mu$ M) 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<sup>[1]</sup>. VS-5584 is a potent inhibitor of mTOR (IC<sub>50</sub>=37 nM) as well as class I PI3K isoforms (IC<sub>50</sub>: PI3K $\alpha$ =16 nM; PI3K $\beta$ =68 nM; PI3K $\gamma$ =25 nM; PI3K $\delta$ =42 nM). All other evaluated kinases show negligible binding when tested up to 10  $\mu$ M VS-5584<sup>[1]</sup>.

**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 stem 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<sup>[1]</sup>. 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<sup>[1]</sup>.



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