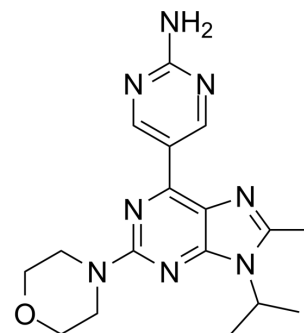


VS-5584

Cat. No.:	HY-16585		
CAS No.:	1246560-33-7		
Molecular Formula:	C ₁₇ H ₂₂ N ₈ O		
Molecular Weight:	354.41		
Target:	PI3K; mTOR		
Pathway:	PI3K/Akt/mTOR		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 33.33 mg/mL (94.04 mM; Need ultrasonic)

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.8216 mL	14.1080 mL	28.2159 mL
	5 mM	0.5643 mL	2.8216 mL	5.6432 mL
	10 mM	0.2822 mL	1.4108 mL	2.8216 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (7.05 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (7.05 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (7.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

VS-5584 is a pan-PI3K/mTOR kinase inhibitor with IC₅₀s 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

IC ₅₀ & Target	PI3Kα	PI3Kγ	PI3Kδ	PI3Kβ
	16 nM (IC ₅₀)	25 nM (IC ₅₀)	42 nM (IC ₅₀)	68 nM (IC ₅₀)
	Vps34	mTOR	mTORC1	mTORC2
	7470 nM (IC ₅₀)	37 nM (IC ₅₀)		

	DNA-PK 1270 nM (IC ₅₀)
In Vitro	<p>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 (IC₅₀=37 nM) as well as class I PI3K isoforms (IC₅₀: 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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
In Vivo	<p>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^[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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

PROTOCOL

Cell Assay ^[1]	<p>For proliferation assays in 96-well plates, SET-2, SNU-478, SNU-1196, SNU-245, SNU-1079, SNU-308, SNU-869, and MKN7 cells are used. The multiple myeloma cells (H929, MM1.S, MM1.R, R8226, U266) and nasopharyngeal cells (CNE-1, CNE-2, HONE1, HK1) are used. Cells are seeded at 30% to 50% confluency for adherent cells, or 2,000 to 6,000 cells for suspension cells and treated the following day with VS-5584 (in triplicates) at concentrations up to 10 μM for 48 hours. Cell viability is monitored using the CellTiter-Glo assay. Dose-response curves were plotted to determine IC₅₀ values for the compounds using the XL-fit software^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
Animal Administration ^[1]	<p>Mice^[1]</p> <p>Athymic BALB/c nude mice (BALB/cOlaHsd-Foxn1nu) are used. Fox-Chase severe combined immunodeficient (SCID) mice (CB17/lcr-Prkdc^{scid}/CrIBltw) are used. Male (PC3 and COLO 205) or female (MV4-11 and HuH7) BALB/c nude mice or female SCID mice (NCI-N87) are implanted intradermally in the right flank with 5×10⁶ (PC3, COLO205, HuH7, NCI-N87) or 1×10⁷ (MV4-11) cells. Cells are resuspended in 70% (v/v; COLO205 and HuH7 only) or 50% (v/v) serum-free growth medium/Matrigel and injected in a total volume of 100 μL, using a 27.5-gauge needle. Dosing started 7 to 14 days after tumor implantation. VS-5584 (11 and 25 mg/kg) is dosed daily orally^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

CUSTOMER VALIDATION

- Research Square Preprint. 2020 Sep.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Hart S, et al. VS-5584, a novel and highly selective PI3K/mTOR kinase inhibitor for the treatment of cancer. Mol Cancer Ther, 2013, 12(2), 151-161.

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

India Contact:

Life Technologies (India) Pvt. Ltd.

306, Aggarwal City Mall, Opposite M2K Pitampura, Delhi – 110034 (INDIA). Ph: +91-11-42208000, 42208111, 42208222, Mobile: +91-9810521400, Fax: +91-11-42208444

Email: customerservice@lifetechindia.com Website: www.lifetechindia.com