产品名称：SGI-1776 free base
产品别名：SGI-1776

生物活性：

Description	SGI-1776 is an inhibitor of **Pim** kinases, with **IC_{50}**s of 7 nM, 363 nM, and 69 nM for Pim-1, -2 and -3, respectively.
IC_{50} & Target	Ki: 7 nM (Pim-1), 363 nM (Pim-2), 69 nM (Pim-3)[4]
In Vitro	causes cell cycle arrest and reduces cell proliferation in SACC-83 and SACC-LM cells. SGI-1776 (5 μM) inhibits cell migration and invasiveness in both SACC-83 and SACC-LM cells. SGI-1776 (0, 2.5, or 5 μM) induces apoptosis via Caspase-3 activation[1]. SGI-1776 (5 μM) exerts inhibitory effects on both lipid accumulation and TG synthesis without affecting the number of adipocytes. SGI-1776 (5 μM) inhibits adipogenesis particularly at an early phase of differentiation. SGI-1776 (5 μM) decreases the expression of C/EBP-α and PPAR-γ and the phosphorylation levels of STAT-3 during adipocyte differentiation, and downregulates the protein and/or mRNA expression of FAS, leptin and RANTES during adipocyte differentiation[2]. SGI-1776 shows the significant activity against HO-8910 cells in a dose-dependent manner, with IC_{50} of (5.2±0.6) μM, and the inhibiting effect of SGI-1776 is sharply increased from 1.25 μM to 20 μM in vitro. SGI-1776 inhibits the migration and invasion of HO-8910 cells in a dose-dependent manner, and the inhibiting migration and invasion rate of 5 μM. SGI-1776 (2.5, 5 and 10 μM) decreases Pim-1 kinase activity of HO-8910 cells in a dose-dependent manner. Furthermore, the down-regulation of Pim-1 expression by SGI-1776 significantly inhibits cell viability, arrests cell in G1 phase, and inhibits the migration and invasion[3].
In Vivo	SGI-1776 (75, 200 mg/kg, p.o.) shows potent and sustained antitumor activity in a dose dependent manner in MV-4-11 xenografts[4].
Solvent&Solubility	***In Vitro:*** **DMSO： 125 mg/mL (308.32 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4666 mL	12.3329 mL	24.6658 mL
	5 mM	0.4933 mL	2.4666 mL	4.9332 mL
	10 mM	0.2467 mL	1.2333 mL	2.4666 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.08 mg/mL (5.13 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (5.13 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；

	向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.08 mg/mL (5.13 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (5.13 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.08 mg/mL (5.13 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (5.13 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Hou X, et al. Biochemical changes of salivary gland adenoid cystic carcinoma cells induced by SGI-1776. Exp Cell Res. 2017 Mar 15;352(2):403-411. [2]. Park YK, et al. The novel anti-adipogenic effect and mechanisms of action of SGI-1776, a Pim-specific inhibitor, in 3T3-L1 adipocytes. Int J Mol Med. 2016 Jan;37(1):157-64 [3]. Xie J, et al. SGI-1776, an imidazo pyridazine compound, inhibits the proliferation of ovarian cancer cells by inactivating Pim-1. Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2014 Jul;39(7):649-57 [4]. Chen LS, et al. Mechanisms of cytotoxicity to Pim kinase inhibitor, SGI-1776, in acute myeloid leukemia. Blood, 2011, 118(3), 693-702.

实验参考：

Cell Assay	Cells are seeded in a 96-well plate at a density of 5 000 cells/well. After incubation for 24 h, different concentrations of SGI-1776 (0.625, 1.25, 2.5, 5, 10, 20, 40 μM) are added to each well and cultured for 48 h. The medium is removed and then incubated with 5 mg/L MTT for 4 h. Next, the supernatant is removed after centrifugation. Finally, 100 μL of DMSO is added and an absorbance at 570 nm wavelength (A570) is measured by enzyme-labeling instrument. Relative cell proliferation inhibition rate (IR)=(1-average A570 of the experimental group/average A570 of the control group)×100%.[3]
Animal Administration	The conditions for animal room environment and photoperiod are 20-25°C, 40%-70% humidity, and 12 hours of light/12 hours of dark cycle. Each mouse is inoculated subcutaneously at the right flank with MV-4-11 tumor cells (5×10^6). The treatments start when the tumor size reach 80-150 mm^3. Mice are randomized to treatment groups based on their tumor sizes; tumor size is measured in 2 dimensions using a caliper, and the volume is expressed in mm^3 using the formula: $V = 0.5\ a \times b^2$ where a and b are the long and short diameters of the tumor, respectively. Pretreatment randomization ensures that each group has approximately the same mean tumor size. Mice are treated with vehicle (5% dextrose), SGI-1776 or cytarabine (ara-C). SGI-1776 and ara-C are formulated in 5% dextrose. SGI-1776 is administered by oral gavage (PO) on a daily × 5/week or twice/week schedule; ara-C is administered by intraperitoneal injection 3 times/week for 3 consecutive weeks. Animals are euthanized when their measured tumor size is greater than 3000 mm^3 or when they lose ≥ 20% initial body weight; if the body weight loss ≥ 15%, treatment is stopped at first until mice regain body weight. Mice are euthanized when body weight loss is still ≥ 20% even after stopping treatment. T/C value (in %) is an indication of antitumor efficacy, where T

	and C are the mean tumor volume of the treated and control groups, respectively, on a given day. The differences between the mean tumor sizes for comparing groups is analyzed using the ANOVA test, where $P \leq 0.05$ is considered to be statistically significant. [4]
Kinase Assay	SACC-83 and SACC-LM cells of 0 μM, 2.5 μM and 5 μM groups after SGI-1776 exposure are harvested. 6 samples of SACC cells are diluted in Kinase buffer and pipetted into the wells which is pre-coated with a substrate corresponding to recombinant p21waf1. It contains threonine residues that can be efficiently phosphorylated by Pim-1. After undergoing the procedure, measure absorbance in each well is quantitated by spectrophotometry at dual wavelengths of 450/540 nm. It reflects the relative amount of Pim-1 activity in the 6 groups of SACC cells. [1]
References	[1]. Hou X, et al. Biochemical changes of salivary gland adenoid cystic carcinoma cells induced by SGI-1776. Exp Cell Res. 2017 Mar 15;352(2):403-411. [2]. Park YK, et al. The novel anti-adipogenic effect and mechanisms of action of SGI-1776, a Pim-specific inhibitor, in 3T3-L1 adipocytes. Int J Mol Med. 2016 Jan;37(1):157-64 [3]. Xie J, et al. SGI-1776, an imidazo pyridazine compound, inhibits the proliferation of ovarian cancer cells by inactivating Pim-1. Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2014 Jul;39(7):649-57 [4]. Chen LS, et al. Mechanisms of cytotoxicity to Pim kinase inhibitor, SGI-1776, in acute myeloid leukemia. Blood, 2011, 118(3), 693-702.