产品名称：SD-208
产品别名：SD-208

生物活性：

Description	SD-208 is a selective TGF-βRI (ALK5) inhibitor with IC_{50} of 48 nM, and > 100-fold selectivity over TGF-βRII.
IC_{50} & Target	IC50: 48 nM (TGF-βRI)
In Vitro	SD-208 inhibits the cell growth and constitutive and TGF-beta-evoked migration and invasion, and enhances immunogenicity in murine SMA-560 and human LN-308 glioma cells[1]. SD-208 blocks TGF-beta-induced phosphorylation of the receptor-associated Smads, Smad2 and Smad3, and stimulates epithelial-to-mesenchymal transdifferentiation, migration, and invasiveness into Matrigel in vitro[2]. SD-208 also abolishes the promoting effect of TGF-β on neointimal smooth muscle-like cell (SMLC) proliferation and migration in vitro[3].
In Vivo	SD-208 (1 mg/mL, p.o.) significantly prolongs the median survival of SMA-560 glioma-bearing mice[1]. In syngeneic 129S1 mice, SD-208 (60 mg/kg/d, p.o.) inhibits primary R3T tumor growth, and reduces the number and the size of lung metastases[2]. In the murine aortic allograft model, SD-208 effectively reduces the formation of intimal hyperplasia of transplant arteriosclerosis (TA)[3].
Solvent&Solubility	***In Vitro:*** **DMSO : 9.09 mg/mL (25.77 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8349 mL	14.1743 mL	28.3487 mL
5 mM	0.5670 mL	2.8349 mL	5.6697 mL
10 mM	0.2835 mL	1.4174 mL	2.8349 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: 0.91 mg/mL (2.58 mM); Suspended solution; Need ultrasonic

此方案可获得 0.91 mg/mL (2.58 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

以 1 mL 工作液为例，取 100 μL 9.1 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: 0.91 mg/mL (2.58 mM); Suspended solution; Need ultrasonic

	此方案可获得 0.91 mg/mL (2.58 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 9.1 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: ≥ 0.91 mg/mL (2.58 mM); Clear solution 此方案可获得 ≥ 0.91 mg/mL (2.58 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 9.1 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Uhl M, et al. SD-208, a novel transforming growth factor beta receptor I kinase inhibitor, inhibits growth and invasiveness and enhances immunogenicity of murine and human glioma cells in vitro and in vivo. Cancer Res. 2004 Nov 1;64(21):7954-61. [2]. Ge R, et al. Inhibition of growth and metastasis of mouse mammary carcinoma by selective inhibitor of transforming growth factor-beta type I receptor kinase in vivo. Clin Cancer Res. 2006 Jul 15;12(14 Pt 1):4315-30. [3]. Sun Y, et al. Inhibition of intimal hyperplasia in murine aortic allografts by the oral administration of the transforming growth factor-beta receptor I kinase inhibitor SD-208. J Heart Lung Transplant. 2014 Jun;33(6):654-61.

实验参考：

Cell Assay	Glioma cells are cultured in the absence or presence of SD-208 (1 μM) for 48 hours. The cells are pulsed for the last 24 hours with [methyl-^{3}H]thymidine (0.5 μCi) and harvested, and incorporated radioactivity is determined in a liquid scintillation counter. [1]
Animal Administration	VM/Dk mice are purchased from the TSE Resource Center. Mice of 6 to 12 weeks of age are used for the survival experiments. Groups of eight mice are anesthesized before all intracranial procedures and placed in a stereotaxic fixation device. A burr hole is drilled in the skull 2 mm lateral to the bregma. The needle of a Hamilton syringe is introduced to a depth of 3 mm. SMA-560 cells [5×10^{3}cells] resuspended in a volume of 2 μL of PBS are injected into the right striatum. Three days later, the mice are allowed to drink SD-208 at 1 mg/mL in deionized water. The mice are observed daily and, in the survival experiments, sacrificed on development of neurologic symptoms. [1]
Kinase Assay	Various kinase activities are assayed by measuring the incorporation of radiolabeled ATP into a peptide or protein substrate. The reactions are performed in 96-well plates and included the relevant kinase, substrate, ATP, and appropriate cofactors. The reactions are incubated and then stopped by the addition of phosphoric acid. Substrate is captured onto a phosphocellulose filter, which is washed free of unreacted ATP. The counts incorporated are determined by counting on a microplate scintillation counter. The ability of SD-208 to inhibit the respective kinase is determined by comparing counts incorporated in the presence of compound with those incorporated in the absence of compound. [1]
References	[1]. Uhl M, et al. SD-208, a novel transforming growth factor beta receptor I kinase inhibitor, inhibits growth and invasiveness and enhances immunogenicity of murine and human glioma cells in vitro and in vivo. Cancer Res. 2004 Nov 1;64(21):7954-61. [2]. Ge R, et al. Inhibition of growth and metastasis of mouse mammary carcinoma by selective inhibitor of transforming growth factor-beta type I receptor kinase in vivo. Clin Cancer Res. 2006 Jul

	15;12(14 Pt 1):4315-30. [3]. Sun Y, et al. Inhibition of intimal hyperplasia in murine aortic allografts by the oral administration of the transforming growth factor-beta receptor I kinase inhibitor SD-208. J Heart Lung Transplant. 2014 Jun;33(6):654-61.