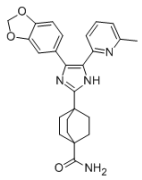
SM 16

Cat. No.:	HY-111482
CAS No.:	614749-78-9
Molecular Formula:	$C_{25}H_{26}N_4O_3$
Molecular Weight:	430.5
Target:	TGF-β Receptor
Pathway:	TGF-beta/Smad

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 : 65 mg/mL (150.99 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3229 mL	11.6144 mL	23.2288 mL
5 mM	0.4646 mL	2.3229 mL	4.6458 mL
10 mM	0.2323 mL	1.1614 mL	2.3229 mL

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

In Vivo

1. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: ≥ 2.58 mg/mL (5.99 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline**
   Solubility: ≥ 2.58 mg/mL (5.99 mM); Clear solution
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 2.58 mg/mL (5.99 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SM 16 is a **ALK5/ALK4** kinase inhibitor with **K_i**s of 10 and 1.5 nM, respectively.

IC_{50} & Target

Ki: ALK5 (10 nM), ALK4 (1.5 nM)[1]

In Vitro

SM 16 inhibits TGFβ-induced plasminogen activator inhibitor-luciferase activity (IC_{50}=64 nM) and TGFβ- or activin-induced Smad2 phosphorylation at concentrations between 100 and 620 nM. SM 16 is tested against >60 related and

	unrelated kinases and shows moderate off-target activity only against Raf (IC_{50}=1 μM) and p38/SAPKa (IC_{50}=0.8 μM). SM 16 exhibits no inhibitory activity against ALK family members ALK1 and ALK6[1].
In Vivo	SM 16 penetrates tumor cells in vivo, suppressing tumor phosphorylated Smad2/3 levels for at least 3 h following treatment of tumor-bearing mice with a single i.p. bolus of 20 mg/kg SM 16. The growth of established AB12 tumors is significantly inhibited by 5 mg/kg/d SM 16 (P<0.001) delivered via s.c. miniosmotic pumps over 28 days[1].

PROTOCOL

Animal Administration [1]

Mice[1]

BALB/c mice are injected on the right flank with 1×10^6 AB12 tumor cells. Mice are randomly divided into two groups and one group is implanted with minipumps loaded with 20% Captisol (control) on the left flank and the other group is implanted with minipumps loaded with 20 mg/mL SM 16. Tumor recurrence is defined as the first day when a tumor is unambiguously visible or palpable. Plasma is obtained under anesthesia and analyzed for SM 16[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Suzuki E, et al. A novel small-molecule inhibitor of transforming growth factor beta type I receptor kinase (SM16) inhibits murine mesothelioma tumor growth in vivo and prevents tumor recurrence after surgical resection. Cancer Res. 2007 Mar 1;67(5):2351-9.

[2]. Fu K, et al. SM16, an orally active TGF-beta type I receptor inhibitor prevents myofibroblast induction and vascular fibrosis in the rat carotid injury model. Arterioscler Thromb Vasc Biol. 2008 Apr;28(4):665-71.

[3]. Engebretsen KV, et al. Attenuated development of cardiac fibrosis in left ventricular pressure overload by SM16, an orally active inhibitor of ALK5. J Mol Cell Cardiol. 2014 Nov;76:148-57.

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