产品名称：GKT137831
产品别名：Setanaxib；GKT831

生物活性：

Description	Setanaxib (GKT137831) is a selective NADPH oxidase (NOX1/4) inhibitor with Kis of 140 and 110 nM, respectively.
IC_{50} & Target	Ki: 140±40 nM (Nox1), 1750±700 nM (Nox2), 110±30 nM (Nox4), 410±100 nM(Nox5)[1]
In Vitro	Setanaxib (GKT137831) is a potent Nox1/4 inhibitor (Kis=140±40/110±30 nM) [1]. Administration of Setanaxib (GKT137831) throughout the 72-hour period of normoxia or hypoxia exposure attenuates HPASMC proliferation under normoxic conditions at the 20 μM concentration but had no effect on proliferation in normoxic HPAECs. In the prevention paradigm, Setanaxib (GKT137831) attenuates hypoxia-induced HPASMC and HPAEC proliferation at 5 and 20 μM. Complementary assays of cell proliferation measuring the expression of PCNA or manual cell counting confirmed that Setanaxib (GKT137831) attenuates hypoxia-induced pulmonary vascular cell proliferation[2]
In Vivo	During the last half of CCl4 injections, some mice are treated with Setanaxib (GKT137831) daily. CCl4-induced liver fibrosis is more pronounced in SOD1mu compared to WT mice. Liver fibrosis in both SOD1mu and WT mice is attenuated by Setanaxib (GKT137831) treatment. The increased hepatic α-SMA expression is markedly decreased in SOD1mu mice treated with Setanaxib (GKT137831), to a level similar to that of WT mice given the NOX1/4 inhibitor[1]

Solvent&Solubility

In Vitro:

DMSO : 14.29 mg/mL (**36.19 mM**; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5326 mL	12.6630 mL	25.3261 mL
	5 mM	0.5065 mL	2.5326 mL	5.0652 mL
	10 mM	0.2533 mL	1.2663 mL	2.5326 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: ≥ 1.43 mg/mL (3.62 mM); Clear solution

此方案可获得 ≥ 1.43 mg/mL (3.62 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 14.299999 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: 1.43 mg/mL (3.62 mM); Precipitated solution; Need ultrasonic 此方案可获得 1.43 mg/mL (3.62 mM) 以 1 mL 工作液为例，取 100 μL 14.299999 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。
References	[1]. Aoyama T, et al. Nicotinamide adenine dinucleotide phosphate oxidase in experimental liver fibrosis: GKT137831 as a novel potential therapeutic agent. Hepatology. 2012 Dec;56(6):2316-27. [2]. Green DE, et al. The Nox4 inhibitor GKT137831 attenuates hypoxia-induced pulmonary vascular cell proliferation. Am J Respir Cell Mol Biol. 2012 Nov;47(5):718-26.

实验参考：

Cell Assay	Monolayers of HPAECs and HPASMCs are propagated in culture and placed in normoxic (21% O_2, 5% CO_2) or hypoxic (1% O_2, 5% CO_2) conditions for 72 hours. Setanaxib (GKT137831) (0.1-20 μM), or vehicle (1% DMSO) are added to the culture medium at the onset (prevention regimen) or during the last 24 hours (intervention regimen) of a 72-hour hypoxia exposure regimen[2].
Animal Administration	Mice[1] Specific pathogen-free, wild-type (WT) C57BL/6J mice are used. For the carbon tetrachloride (CCl_4) model of liver fibrosis, 6 week old male mice are injected intraperitoneally with CCl_4, which is diluted 1:3 in corn oil, or with vehicle (corn oil) at a dose of 0.5 μL/g of body weight twice a week for a total of 12 injections. During the last half of CCl_4treatment, mice are treated with 60 mg/kg of the NOX1/4 inhibitor Setanaxib (GKT137831) or vehicle by intragastric injection daily. Mice are sacrificed 48 hours after the last CCl_4 injection. For the bile duct ligation (BDL) model, 6 week old male mice are anesthetized. After laparotomy, the common bile duct is ligated twice and the abdomen closed. The sham operation is performed similarly without BDL. From 11 days after operation, mice are treated with 60 mg/kg of the NOX1/4 inhibitor Setanaxib (GKT137831) or vehicle by daily intragastric lavage. Mice are sacrificed 21 days after operation. Serum levels of alanine aminotransferase (ALT) are measured with a commercial kit.
References	[1]. Aoyama T, et al. Nicotinamide adenine dinucleotide phosphate oxidase in experimental liver fibrosis: GKT137831 as a novel potential therapeutic agent. Hepatology. 2012 Dec;56(6):2316-27. [2]. Green DE, et al. The Nox4 inhibitor GKT137831 attenuates hypoxia-induced pulmonary vascular cell proliferation. Am J Respir Cell Mol Biol. 2012 Nov;47(5):718-26.