上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：N-Desmethyl-riociguat
产品别名：Nelociguat；BAY60-4552

生物活性：

Description	Nelociguat (BAY60-4552) is a nitric oxide sensitive soluble guanylate cyclase stimulator.
In Vitro	Soluble guanylate cyclase (sGC) is a key enzyme in the nitric oxide (NO) signalling pathway[1]. Riociguat is metabolized to BAY60-4552 not only via cytochrome P450 isoenzymes 3A4 (CYP3A4), CYP2C8, and CYP2J2, but also via CYP1A1, located in the liver and lungs[2].
In Vivo	GSK2181236A and BAY 60-4552 provide partial benefit against hypertension-induced end-organ damage. In spontaneously hypertensive stroke-prone rats, a low dose of BAY 60-4552 decreases urine output and improved survival. A high dose also reduces urine output, and in addition reduces microalbuminuria and attenuates the increase in mean arterial pressure. Both the 0.3 and 3 mg/kg/day doses of BAY 60-4552 improves survival of 46 and 69%. Seven weeks of treatment with BAY 60-4552 (0.3 and 3.0 mg/kg/day) dose-dependently decreases urine output to 79±11 and 56±10 mL/day[1]. BAY 60-4552, and vardenafil provides synergistic beneficial effects and might therefore salvage patients who experience treatment failures with PDE5 inhibitors after radical prostatectomy[3].
Solvent&Solubility	***In Vitro:*** **DMSO : 105 mg/mL** (**257.11 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4486 mL	12.2432 mL	24.4864 mL
	5 mM	0.4897 mL	2.4486 mL	4.8973 mL
	10 mM	0.2449 mL	1.2243 mL	2.4486 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: ≥ 2.67 mg/mL (6.54 mM); Clear solution

此方案可获得 ≥ 2.67 mg/mL (6.54 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 26.7 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: ≥ 2.67 mg/mL (6.54 mM); Clear solution

	此方案可获得 ≥ 2.67 mg/mL (6.54 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 26.7 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]. Costell MH, et al. Comparison of soluble guanylate cyclase stimulators and activators in models of cardiovascular disease associated with oxidative stress. Front Pharmacol. 2012 Jul 5;3:128. [2]. Zhao X, et al. Pharmacokinetics of the Soluble Guanylate Cyclase Stimulator Riociguat in Healthy Young Chinese Male Non-Smokers and Smokers: Results of a Randomized, Double-Blind, Placebo-Controlled Study. Clin Pharmacokinet. 2016 May;55(5):615-24. [3]. Oudot A, et al. Combination of BAY 60-4552 and vardenafil exerts proerectile facilitator effects in rats with cavernous nerve injury: a proof of concept study for the treatment of phosphodiesterase type 5 inhibitor failure. Eur Urol. 2011 Nov;60(5):1020-6.

实验参考：

Animal Administration	Rats: Rats are orally gavaged with vehicle (0.5% HPMC, 5% DMSO, and 0.1% Tween 80; 10 mL/kg; n=14), GSK2181236A (0.1 or 1.0 mg/kg; n=11-14), or BAY 60-4552 (0.3 or 3.0 mg/kg; n=10-12) 2 h prior to ischemia. Blood is collected at the initiation of ischemia and after 24 h reperfusion. Plasma is obtained for analysis[1].
References	[1]. Costell MH, et al. Comparison of soluble guanylate cyclase stimulators and activators in models of cardiovascular disease associated with oxidative stress. Front Pharmacol. 2012 Jul 5;3:128. [2]. Zhao X, et al. Pharmacokinetics of the Soluble Guanylate Cyclase Stimulator Riociguat in Healthy Young Chinese Male Non-Smokers and Smokers: Results of a Randomized, Double-Blind, Placebo-Controlled Study. Clin Pharmacokinet. 2016 May;55(5):615-24. [3]. Oudot A, et al. Combination of BAY 60-4552 and vardenafil exerts proerectile facilitator effects in rats with cavernous nerve injury: a proof of concept study for the treatment of phosphodiesterase type 5 inhibitor failure. Eur Urol. 2011 Nov;60(5):1020-6.