产品名称：(S)-6,7-二氢-2-硝基-6-[[4-(三氟甲氧基)苯基]甲氧基]-5H-咪唑并[2,1-B][1,3]恶嗪

产品别名：Pretomanid

生物活性：

Description	Pretomanid (PA-824) is a small-molecule nitroimidazopyran drug candidate for the treatment of tuberculosis; the MIC values of PA-824 against a panel of MTB pan-sensitive and rifampin mono-resistant clinical isolates ranged from 0.015 to 0.25 ug/ml. IC50 value: 0.015 to 0.25 ug/ml (MICs) [1]
IC_{50} & Target	Tuberculosis.
In Vitro	Pretomanid (PA-824) exhibited a sub-micromolar minimal inhibitory concentration (MIC) against MTB, Although Pretomanid (PA-824) was not the most potent NAP against cultured MTB clinical isolates, it was the most active in infected mice when orally administered at 25 mg/kg. This indicated that Pretomanid (PA-824) might possess more desirable pharmacokinetic properties than the other more potent NAP compounds that we tested. Further studies in mice at 25, 50 and 100 mg kg-1 Pretomanid (PA-824) daily for 10 days resulted in reductions of mycobacterial burden in both spleen and lung tissues that were comparable to that of INH at 25 mg kg -1 [1]. Pretomanid (PA-824) showed significant activity at 2, 10, and 50 microg/ml, similar to that of metronidazole, in a dose-dependent manner. Pretomanid (PA-824) at 100 mg/kg in cyclodextrin/lecithin was as active as moxifloxacin at 100 mg/kg and isoniazid at 25 mg/kg and was slightly more active than rifampin at 20 mg/kg. Long-term treatment with Pretomanid (PA-824) at 100 mg/kg in cyclodextrin/lecithin reduced the bacterial load below 500 CFU in the lungs and spleen [2]. Pretomanid (PA-824) has no effect on the viability of M. leprae in all three models, consistent with the lack of the nitroimidazo-oxazine-specific nitroreductase, encoded by Rv3547 in the M. leprae genome, which is essential for activation of this molecule [3].
Solvent&Solubility	***In Vitro:*** **DMSO : 20 mg/mL (55.67 mM; ultrasonic and warming and heat to 80°C)**

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7835 mL	13.9175 mL	27.8350 mL
	5 mM	0.5567 mL	2.7835 mL	5.5670 mL
	10 mM	0.2783 mL	1.3917 mL	2.7835 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 mg/mL (5.57 mM); Clear solution

此方案可获得 ≥ 2 mg/mL (5.57 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 20.0 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 mg/mL (5.57 mM); Clear solution 此方案可获得 ≥ 2 mg/mL (5.57 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.0 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 mg/mL (5.57 mM); Clear solution 此方案可获得 ≥ 2 mg/mL (5.57 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 20.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Stover CK, et al. A small-molecule nitroimidazopyran drug candidate for the treatment of tuberculosis. Nature. 2000 Jun 22;405(6789):962-6. [2]. Lenaerts AJ, et al. Preclinical testing of the nitroimidazopyran PA-824 for activity against Mycobacterium tuberculosis in a series of in vitro and in vivo models. Antimicrob Agents Chemother. 2005 Jun;49(6):2294-301. [3]. Manjunatha UH, et al. Mycobacterium leprae is naturally resistant to PA-824. Antimicrob Agents Chemother. 2006 Oct;50(10):3350-4.