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产品名称：BTZ043
产品别名：BTZ043

生物活性：

Description	BTZ043 is an inhibitor of decaprenyl-phosphoribose-epimerase (DprE1), with MICs of of 2.3 nM and 9.2 nM for M. tuberculosis H37Rv and Mycobacterium smegmatis, respectively.
IC_{50} & Target	DprE1[1].
In Vitro	The MIC of BTZ043 against M. tuberculosis H37Rv and Mycobacterium smegmatis are 1 ng/mL (2.3 nM) and 4 ng/mL (9.2 nM), respectively[2]. The in vitro activity of BTZ043 against 30 Nocardia brasiliensis isolates is also tested. The MIC50 and MIC90 values for BTZ043 are 0.125 and 0.25 μg/mL. The MIC for N. carnea ATCC 6847 is 0.003μg/mL, for N. transvalensis ATCC 6865 is 0.003μg/mL, for N. brasiliensis NCTC10300 is 0.03 μg/mL, and for N. brasiliensis HUJEG-1 is 0.125μg/mL. The MIC value for M. tuberculosis H37Rv is 0.000976 μg/mL. The MIC value of BTZ-043 is >64 μg/mL for Escherichia coli ATCC 25922 and S. aureus ATCC 29213[3].
In Vivo	Four weeks of treatment with BTZ043 reduces the bacterial burden in the lungs and spleens by 1 and 2 logs, respectively, at the concentrations used. Additional results suggest that BTZ043 efficacy is time-rather than dose-dependent. Acute (5 g/kg) and chronic (25 and 250 mg/kg) toxicology studies in uninfected mice show that, even at the highest dose tested, there are no adverse anatomical, behavioral, or physiological effects after one month[2].

Solvent&Solubility

In Vitro:

DMSO : 13.3 mg/mL (30.83 mM; Need ultrasonic and warming)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3181 mL	11.5904 mL	23.1809 mL
	5 mM	0.4636 mL	2.3181 mL	4.6362 mL
	10 mM	0.2318 mL	1.1590 mL	2.3181 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: 2.5 mg/mL (5.80 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (5.80 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 25.0 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: 2.5 mg/mL (5.80 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (5.80 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 25.0 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: ≥ 2.5 mg/mL (5.80 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.80 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Vadim Makarov et al. The 8-Pyrrole-Benzothiazinones Are Noncovalent Inhibitors of DprE1 fromMycobacterium tuberculosis. Antimicrob Agents Chemother, 2015 Aug, 59(8): 4446-4452. [2]. Makarov V, et al. Benzothiazinones kill Mycobacterium tuberculosis by blocking arabinan synthesis. Science. 2009 May 8;324(5928):801-4. [3]. Norma Alejandra González-Martínez et al. In Vivo Activity of the Benzothiazinones PBTZ169 and BTZ043 against Nocardia brasiliensis. PLoS Negl Trop Dis, 2015 Oct, 9(10): e0004022.

实验参考：

Animal Administration	Mice[2] Animal efficacy is determined in a standard mouse infection model. BALB/c mice are infected with a low bacillary load (~200 CFU) of M. tuberculosis H37Rv via aerosol. Treatment started four-weeks post infection. Mice are dosed by gavage with 37.5, or 300 mg of BTZ043, per kg body weight, in carboxymethyl cellulose formulation (0.25%), once daily, six times/week, for four weeks. Control and treated mice are sacrificed, lungs and spleens homogenized and dilutions plated for enumeration of viable bacilli[2].
References	[1]. Vadim Makarov et al. The 8-Pyrrole-Benzothiazinones Are Noncovalent Inhibitors of DprE1 fromMycobacterium tuberculosis. Antimicrob Agents Chemother, 2015 Aug, 59(8): 4446-4452. [2]. Makarov V, et al. Benzothiazinones kill Mycobacterium tuberculosis by blocking arabinan synthesis. Science. 2009 May 8;324(5928):801-4. [3]. Norma Alejandra González-Martínez et al. In Vivo Activity of the Benzothiazinones PBTZ169 and BTZ043 against Nocardia brasiliensis. PLoS Negl Trop Dis, 2015 Oct, 9(10): e0004022.