### Modified Abstract

**Introduction**

There is a dearth of novel antibacterial agents with which to treat serious Gram-positive and Gram-negative infections (1). Of those drugs that are in clinical development, many suffer from one or more of the following shortcomings: narrow activity spectrum, high MICs, significant resistance in vivo and ex vivo, limited oral bioavailability, poor tissue penetration, and high toxicity. Several compounds from the novel RX-04 program were able to protect mice from lethal infection with a single dose. These results add further value to compounds from the RX-04 program, which have already demonstrated efficacy in murine models of pneumonia, meningitis and kidney infection against key bacterial pathogens. **Methods**

Bacteria were prepared for infection studies by inoculating from frozen stocks onto Tryptic Soy Agar plates containing 5% sheep blood, and incubating at 37°C for 18-24 hours, to inoculate Standard Infusion Kits (SIV). For murine infection studies, SIV were prepared by triturating bacteria in 0.9% saline, and then diluting to 10^8 cfu/ml. For murine antibiotic challenge studies, SIV were prepared by diluting bacteria in 0.9% saline to 10^8 cfu/ml.

**Results**

- **Results**
  - **Table 1. Structures and MICs of compounds used in the present studies.**
  - **Table 2. PD50s of RX-04 compounds in lung infection model caused by S. pneumoniae ATCC10813.**
  - **Table 3. MICs of RX-04 compounds in S. pneumoniae ATCC10813 and S. aureus 10653.**
  - **Table 4. MICs of RX-04 compounds in S. aureus 10653 and P. aeruginosa 10653.**

**Conclusion**

Several compounds from the novel RX-04 program were able to protect mice from lethal S. pneumoniae lung infection with a single dose given 4 hours post-infection.

- **Number of infections:** 5
- **Dose:** 1 mg/kg sc dose
- **Results:**
  - **Table 4. MICs of RX-04 compounds in S. aureus 10653 and P. aeruginosa 10653.**

**References**


**Abstract**

Methods

**Results**

- **Table 1. Structures and MICs of compounds used in the present studies.**
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- **Table 3. MICs of RX-04 compounds in S. pneumoniae ATCC10813 and S. aureus 10653.**
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**Conclusion**

Several compounds from the novel RX-04 program were able to protect mice from lethal S. pneumoniae lung infection with a single dose given 4 hours post-infection.

- **One compound profiled in detail, RX-P073, demonstrated good dose-responsive efficacy in terms of lung bacterial burden at 24 hours, compared to untreated controls at the start of therapy, as well as protection from lethality over 5–7 days.**
- **These novel compounds have all demonstrated efficacy in murine preclinical infection models.**

**References**


