Results - Rats

**Dose-Response Study:**
- 120 mg/kg dosing for 10 days in rats given twice a day at 1.5 h interval
- Brain and blood AUC last (µg/mL*h) and AUC/MIC (µg/mL*h) for RX 2382 in Male Han old, male rats

**Dose-Response Study Summary:**
- Brain and blood AUC last (µg/mL*h) and AUC/MIC (µg/mL*h) for RX 2382 in Male Han old, male rats

**Results:**
- Brain and blood AUC last (µg/mL*h) and AUC/MIC (µg/mL*h) for RX 2382 in Male Han old, male rats

**Tissue Levels:**
- Brain and blood AUC last (µg/mL*h) and AUC/MIC (µg/mL*h) for RX 2382 in Male Han old, male rats

**Tissue Levels Summary:**
- Brain and blood AUC last (µg/mL*h) and AUC/MIC (µg/mL*h) for RX 2382 in Male Han old, male rats

**End of Dosing:**
- Brain and blood AUC last (µg/mL*h) and AUC/MIC (µg/mL*h) for RX 2382 in Male Han old, male rats

**Results - Non-Human Primates

**Study Design:**
- 20 male cynomologus macaque monkeys, 2 groups
- 10 monkeys/group
- 10 mg/kg daily dose
- Blood samples collected at specific time points

**Data Summary:**
- Blood samples collected at specific time points

**Results:**
- Blood samples collected at specific time points

**Conclusion:**
- Blood samples collected at specific time points

**ACKNOWLEDGMENTS**

Study designs conducted in collaboration with Dr. Effrosyni V. Oleson and Dr. Steve Weber.

**Anatomical & Clinical Pathology Related to Liver (reference normal ranges shaded):**

**Anatomical & Clinical Pathology Related to Kidney (reference normal ranges shaded):**

**PROGRESS IN THE ESKAPE PATHOGEN PROGRAM: THE EXPLORATORY IN VIVO TOXICOLOGICAL PROFILE OF AN ADVANCED LEAD, RX-P2382**

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**21-24 April 2018**

**POSTER# P0151**

**ABSTRACT**

**INTRODUCTION**

RX-P2382 is a potent and orally bioavailable inhibitor of efflux transporters of the ABC family, which aid in multidrug resistance in bacteria. It has shown promise in treating infections caused by multidrug-resistant pathogens, including ESKAPE pathogens.

**METHODS**

RX-P2382 was evaluated in a detailed pharmacokinetic and toxicology study. The study included acute toxicity and dosing studies in rats and non-human primates, as well as microbiological evaluations. The study was conducted in compliance with GLP and international standards.

**RESULTS**

RX-P2382 demonstrated favorable pharmacokinetic properties, with significant exposure in relevant tissues and organs. However, toxicity was observed with increased exposure, highlighting the importance of dose optimization.

**DISCUSSION**

This study underscores the potential of RX-P2382 as a promising therapeutic agent for combating multidrug-resistant infections. Further optimization is needed to improve safety and efficacy before clinical trials can be initiated.