

BEST-IN-CLASS DAROBACTIN DERIVATIVE AGAINST GRAM-NEGATIVE BACTERIA

Keywords: Peptide antibiotics, ESKAPE, *Pseudomonas aeruginosa*, Gram-negative, *Enterobacteriaceae*, Bama

INVENTION NOVELTY

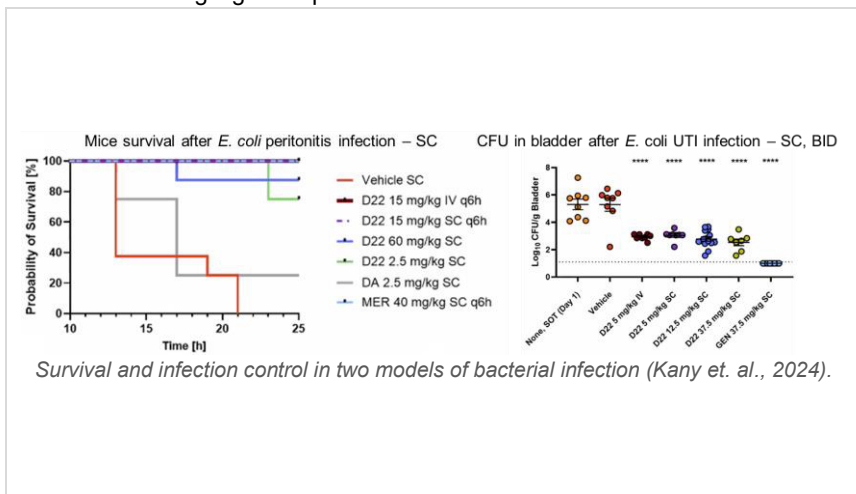
Best-in-class darobactin derivatives with exceptional antibiotic activity against Gram-negative pathogens and an innovative heterologous expression system for efficient, scalable production.

VALUE PROPOSITION

Assets in lead optimization stage to curb AMR in Gram-negative pathogens from the ESKAPE family

- **Production at scale:** Engineered biosynthetic gene cluster in *E. coli* BL21 for optimized production, achieving gram quantities
- **Indications:** cUTI with associated bacteremia caused by *Enterobacteriaceae*, hospitalized lung infections caused by *P. aeruginosa* and other critical Gram-negative pathogens
- **Safety profile:** No cytotoxicity against 9 human cell lines and zebra fish larvae up to 37 µg/mL and 500 µg/mL, respectively. No activity in micronucleus assays up to 200 µM

These features highlight the potential to meet an unmet medical need in ESKAPE pathogens.



TECHNOLOGY DESCRIPTION

- **In vitro activity:** MIC 0.062 µg/mL in *A. baumannii* (NDM-1), 0.25 µg/mL for *P. aeruginosa* (PAO1)
- **In vivo target engagement:** Significant reduction of bacterial load in *E. coli* UTI and *P. aeruginosa* thigh infection, 100% survival in *E. coli* peritonitis/sepsis (15 mg/kg IV/SC) and *A. baumannii* zebrafish model (complete clearance at 10 mg/kg SC)
- **ADME/T:** High murine metabolic and plasma stability (Cl_{int} <11.6 µg/mL/min, plasma $t_{1/2}$ >4h), low PPB (62%)
- **Pharmacokinetics:** High urine levels and tissue exposure in lungs, kidney and thigh

COMMERCIAL OPPORTUNITY

The technology is available for co-development and in-licensing partnerships.

DEVELOPMENT STATUS

Antibiotic activity has been investigated against a broad panel of Gram-negative pathogens including resistant strains. PK and PD against different critical pathogens in diverse models of infection have been provided.

PATENT SITUATION

An international PCT application has been filed (WO2022175443) with priority date of 2021. Applications in the US, JP, IN, EP, CN, CA, and AU are pending. Clean FTO over third-party patents.

FURTHER READING

In vivo activity – [Kany et al. 2024. ACS Infectious Diseases. 10 \(12\).](#)