Current standard-of-care (SOC) drugs for the treatment of MRSA infections are limited to a few drugs, which include vancomycin, daptomycin, and linezolid (1). The essential cell division protein FtsZ has been identified as an appealing new target for the development of antibiotics that can be used to treat infections caused by multidrug-resistant (MDR) bacterial pathogens (2). FtsZ self-polymerizes in a GTP-dependent manner to form a ring-like structure (the Z-ring) that is critical for cell division and organization of other critical components for proteolytic synthesis, septum formation, and cell division (3). The substituted benzamide derivative PC190723 is associated with potent bactericidal activity against *Staphylococcus* sp., including MRSA (4). However, the clinical development of PC190723 has been hindered by poor pharmaco-kinetic and pharmacodynamic properties. We have previously reported the design and characterization of 1st-generation produgs of PC190723 (TXY436 and TXY451) with physico-chemical properties that significantly enhance the ease of formulation in vehicles suitable for in vivo administration (5,6). Here we describe a 2nd-generation polymer (TXA709) of an FtsZ-targeting benzamide compound (TXY707) with enhanced metabolic stability, improved pharmacokinetic properties, and superior in vivo efficacy versus MRSA.

**Oral In Vivo Efficacy of the 1st-Generation Prodrug TXY541 vs. MSSA and MRSA**

**PK Results for TXA709 and Its Hydrolysis Product TXA707**

**In Vivo Efficacy of the 2nd-Generation Prodrug TXA709 vs. MSSA and MRSA**

**Validation of the Cell Division Protein FtsZ as the Bactericidal Target of TXA707**

**REFERENCES**