Antibiotic resistance is an urgent public health threat. The CDC estimates there are approximately 2.8 million new cases of antibiotic-resistant infections annually resulting in 35,000 deaths and billions of dollars in health care costs. The development of new drugs is imperative to combat this crisis and prevent the loss of additional lives from once “curable” diseases. Resazomycins, a novel family of antibiotics, have bactericidal activity against Francisella tularensis and Neisseria gonorrhoeae. One resazomycin, resorufin pentyl ether (RPE), significantly reduces vaginal colonization by N. gonorrhoeae in a mouse model of infection. Repeated administration of RPE, however, fails to clear the infection, in contrast to a single dose of ceftriaxone, an antibiotic commonly used to treat gonorrhea, which clears the infection within 24 hours. Further characterization of resazomycins revealed the efficacy of these compounds is limited by interaction with serum albumin and reduced oxygen concentrations found within mammalian tissues. Therefore, we hypothesize that novel resazurin analogs that maintain antimicrobial activity in the presence of serum albumin and low oxygen will have improved therapeutic efficacy in vivo. To date, two different derivatives of RPE have been synthesized and tested for antimicrobial activity against F. tularensis and N. gonorrhoeae – 1-methyl RPE and 4-methyl RPE. Neither of these compounds inhibited the growth of F. tularensis or N. gonorrhoeae. Next, we plan to prepare a series of ketone derivatives of resazurin to alter the electrophilicity and reduction potential of these compounds and test their efficacy against F. tularensis and N. gonorrhoeae.