SYN-004, A NOVEL STRATEGY TO PROTECT THE GUT MICROBIOME FROM THE DELETERIOUS EFFECTS OF RESIDUAL IV β-LACTAM ANTIBIOTICS

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SYN-004 is a clinical stage oral β-lactamase therapy for use with intravenous (IV) β-lactam antibiotics to preserve the gut microbiome by degrading residual antibiotics excreted into the intestine. The intended indication for this enzyme is prevention of Clostridium difficile infection (CDI) and antibiotic associated diarrhea (AAD). SYN-004 was demonstrated to be safe in two preclinical studies in dogs and to not affect the systemic pharmacokinetics of the intravenous antibiotics. SYN-004 has now been studied in two phase 1 clinical trials, a single-ascending dose study and a multiple-ascending dose study, which demonstrated that oral SYN-004 was safe and well tolerated with negligible systemic availability. Two phase 1b/2a clinical trials have been initiated investigating oral SYN-004 in combination with IV ceftriaxone in healthy subjects with functional ileostomies to determine whether SYN-004, i) degrades intestinal ceftriaxone, ii) has any effect on systemic ceftriaxone, iii) is safe when delivered in combination with ceftriaxone and iv) is functional in the presence of proton pump inhibitors. A phase 2b double-blind, placebo-controlled study in patients receiving treatment with IV ceftriaxone for active infection is planned to start in 2015 to determine whether SYN-004 protects the gut microbiome and prevents opportunistic enteric infections like C. difficile.