

## **SYN-004, A NOVEL STRATEGY TO PROTECT THE GUT MICROBIOME FROM THE DELETERIOUS EFFECTS OF RESIDUAL IV $\beta$ -LACTAM ANTIBIOTICS**

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SYN-004 is a clinical stage oral  $\beta$ -lactamase therapy for use with intravenous (IV)  $\beta$ -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*.