BACKGROUND

• Microbiota-based therapies are demonstrating efficacy in preventing recurrent *Clostridium difficile* infections (rCDI).
• RBX7455 is a first-of-its-kind, lyophilized, non-frozen, orally-administered microbiota-restoring drug candidate that was developed for ease-of-use for rCDI patients.
• Herein we present clinical safety and efficacy of a Phase 1 investigator-sponsored trial of RBX7455 for preventing rCDI.
• In addition, we present an accompanying study of microbiome restoration among trial participants.

CLINICAL TRIAL DESIGN & METHODS

• Prospective, single-center, open-label Phase 1 investigator-initiated trial (NCT02981316).
• Inclusion criteria: >18 years old with documentation of recurrent CDI, at least one recurrence after a primary episode and has completed at least two rounds of standard-care oral antibiotic therapy; *C. difficile* diarrhea resolved, i.e., fewer than 3 watery bowel movements at the time of study enrollment for 48 hours or more; a positive stool test for the last treatment. Treatment failure is defined as: recurrence of diarrhea <8 weeks after completion of RBX7455 treatment, a positive stool test for *C. difficile* within 30 days prior to enrollment and standard *C. difficile* treatment.
• Exclusion criteria: Known history of continued CDI diarrhea despite antibiotic treatment for CDI; requirement of continuous antibiotic therapy for a condition other than CDI; previous fecal transplant; previous treatment with RBX2660; history of inflammatory bowel disease (ulcerative colitis, Crohn’s disease, microscopic colitis), irritable bowel syndrome, chronic diarrhea, celiac disease; colostomy; evidence of active colitis; intended exposure to antibiotics within 6 months after study enrollment; compromised immune system (white blood cell count <1000 cells/μL); current or expected use of systemic steroids.
• Antibiotics were discontinued 24-48 hours prior to first RBX7455 dose.
• Participants received 8 RBX7455 capsules per day for four days (Cohort 1), 8 RBX7455 capsules per day for two days (Cohort 2), or 4 RBX7455 capsules per day for two days (Cohort 3).
• Safety was assessed via a patient diary: in clinic at 1, 4, and 8 weeks and via telephone at 2, 3, between 5-7 weeks, and at 3, 6, 12 and 24 months.
• Success was defined as the absence of CDI at 8 weeks following completion of the last treatment. Treatment failure is defined as: recurrence of diarrhea <8 weeks after completion of RBX7455 treatment, a positive stool test for *C. difficile*, a need for retreatment for CDI, and no other cause for diarrhea.
• Stool samples were collected at baseline and at 7, 30, and 60 days and 24 weeks after treatment.

MICROBIOME ANALYSIS

• Nine (9) RBX7455 drug product samples and 89 stool samples from treatment responders were sequenced using a shallow shotgun method (CoreBiome, Minneapolis, MN).
• Multidimensional scaling analysis was performed on participant and RBX7455 operational taxonomic unit data according to a Bray-Curtis dissimilarity metric with non-metric scaling, and group mean relative taxonomic abundances at the class level were calculated by fitting to a Dirichlet-multinomial distribution.

CONCLUSIONS

• In this open-label, investigator-sponsored Phase 1 study, all RBX7455 dosing regimens were effective at preventing rCDI.
• The RBX7455 safety profile is consistent with results from other clinical trials of microbiota-based therapies.
• Microbiota analysis suggests that RBX7455 restores a healthier microbiome composition.