A LYOPHILIZED, NON-FROZEN, ORAL MICROBIOTA-BASED DRUG RBX7455 IS SAFE, REDUCES *CLOSTRIDIUM DIFFICILE* INFECTION RECURRENCE, AND RESTORES THE MICROBIOME

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Background
Microbiota-based therapeutics can effectively prevent recurrent *Clostridium difficile* infections (rCDI). To broaden access to these therapies, RBX7455—a lyophilized, non-frozen, orally-administered microbiota-restoring drug candidate was developed. Herein we report interim results from two dosing cohorts of an open-label Phase 1 trial of RBX7455 for preventing rCDI.

Methods
Nineteen patients with ≥2 CDI episodes following ≥2 courses of standard-of-care antibiotic therapy were enrolled. Patients received eight RBX7455 capsules for four days (cohort 1) or two days (cohort 2). Success was defined as absence of CDI recurrence through 8 weeks after completion of treatment, and adverse events were monitored during and after treatment.

Patients submitted stool samples prior to treatment and at time points after treatment. Stool samples and representative RBX7455 samples were sequenced using an ultra-shallow shotgun sequencing method (BoosterShot, CoreBiome, Minneapolis, MN). Operational taxonomic unit (OTU) data were grouped by cohort and longitudinally and were compared using a Bray-Curtis dissimilarity calculation. Relative OTU abundances at the class level were compared among time points.

Results
Nine of ten patients in cohort 1 (median age = 67, 90% female, median prior CDI episodes = 2) and seven of nine patients in cohort 2 (median age = 54, 55% female, median prior CDI episodes = 3) were recurrence-free at the 8-week endpoint, an overall efficacy of 87%. A total of 37 non-serious adverse events (AE) were observed, with gastrointestinal AEs (constipation) being most common. There were no serious AEs observed.

Prior to treatment, the taxonomic compositions of responder microbiomes were dissimilar from the RBX7455 composition and were dominated by Gammaproteobacteria and Bacilli. After treatment, patient microbiomes converged toward the RBX7455 composition, with Bacteroidia and Clostridia becoming more predominant (Figure 1). Microbiome changes were comparable among responders in both cohorts, although cohort 1 responders appeared to show more convergence toward RBX7455 within the small sample size evaluated.

Conclusion
At the 8-week time point and across two dosing regimens, RBX7455 had 90% and 78% success preventing rCDI in patients with ≥2 prior CDI episodes, with no serious AEs. For this small observational study, both cohorts showed acceptable outcomes. In addition, RBX7455 appears to restore patient microbiomes toward the RBX7455 composition. Microbiome and safety data collection will continue to 6 months after treatment.

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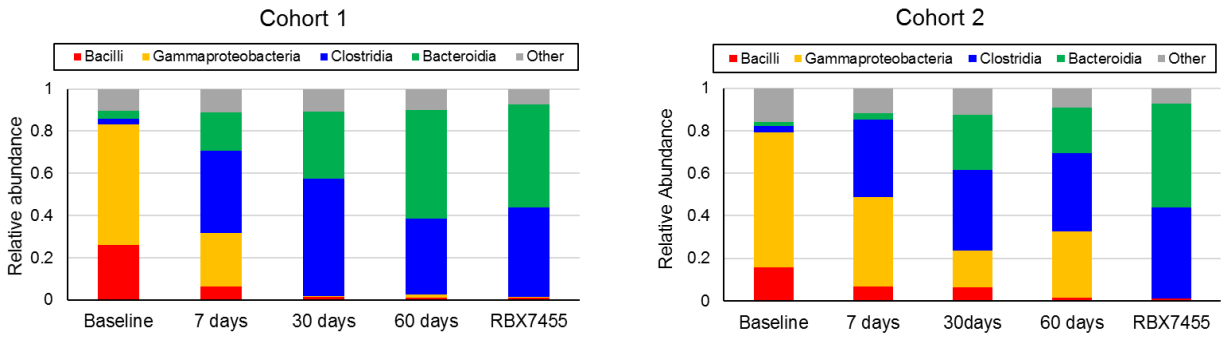

Figure 1. Relative taxonomic abundances at class level for pre- and post-treatment patient samples and for RBX7455.