higher than pre-treatment levels while Gammaproteobacteria and Bacilli declined sharply after treatment, and these changes persisted to at least 24 months.

Conclusion. RBX2660, a microbiota-based drug, was safe and efficacious for preventing rCDI with clinical durability to 24 months after treatment, independent of age or sex, and RBX2660 durability associated with durable microbiome shifts from pre-treatment to a healthier composition.

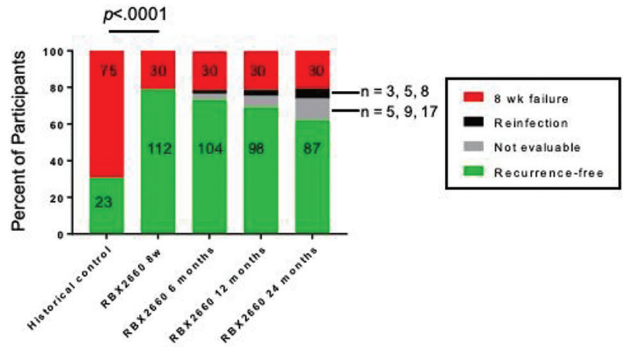

Figure 1: Primary outcome and durability, reported as percentages with number of participants shown as numbers

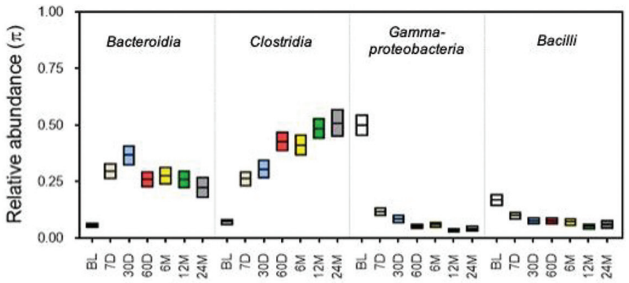

Figure 2: Mean relative abundance (π) with confidence intervals at the taxonomic class level before treatment (BL) and at time points after treatment.

Disclosures. Robert Orenstein, DO, Rebiotix Inc. (Advisor or Review Panel member), Sarah Mische, PhD, Rebiotix Inc. (Employee), Ken Blount, PhD, Rebiotix Inc. (Employee), Lindy Bancke, PharmD, Rebiotix Inc. (Employee), Xin Su, MD, MSci, Rebiotix Inc. (Employee), Dana Walsh, PhD, Rebiotix Inc. (Employee), Adam Harvey, PhD, Rebiotix Inc. (Employee), Carlos Gonzalez, MS, Rebiotix Inc. (Consultant), Dale N. Gerding, MD, Rebiotix Inc. (Board Member).

LB6. EDP-938, a Novel RSV N-Inhibitor, Administered Once or Twice Daily Was Safe and Demonstrated Robust Antiviral and Clinical Efficacy in a Healthy Volunteer Challenge Study

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Session: 83. Late Breaker Oral Abstract Session 1
Thursday, October 3, 2019: 2:35 PM

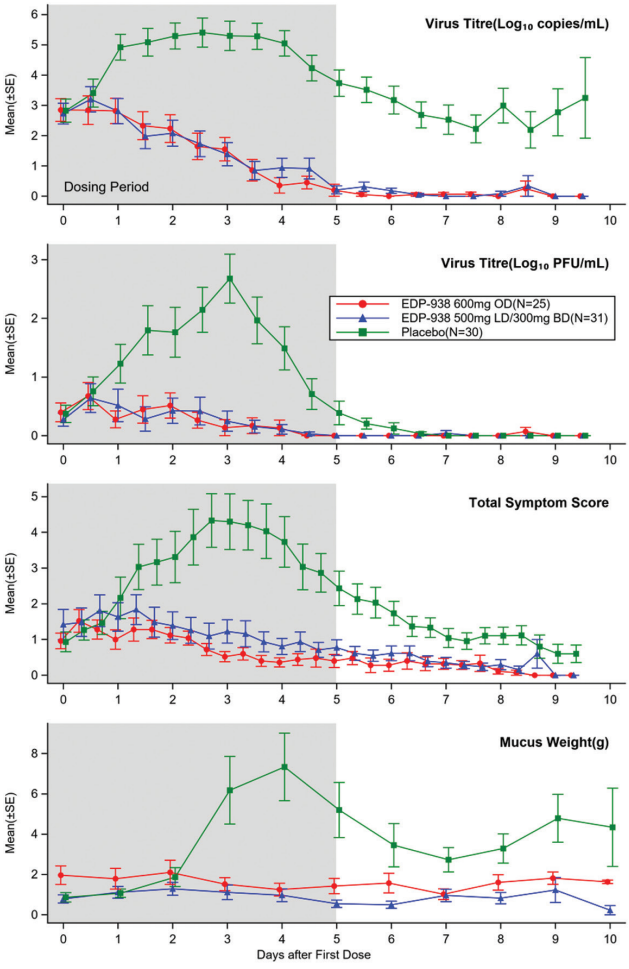
Background. Respiratory syncytial virus (RSV) represents an important global health challenge with significant morbidity and mortality in infants, elderly, and immunocompromised adults. No effective therapy is currently available. EDP-938 demonstrates potent *in vitro* activity against RSV Subtypes A and B. We report data from EDP 938-101, a double-blind, placebo-controlled, Phase 2a study that evaluated EDP-938 in adult volunteers inoculated with RSV-A Memphis 37b.

Methods. Subjects were healthy volunteers, 18–45 years, who were sero-suitable (i.e., lower 25th percentile). After RSV inoculation on Study Day 0, subjects had 12 hourly nasal wash monitored for RSV infection by qualitative RSV RT–PCR. On Study Day 5 or previously if qualitative RT–PCR was RSV+, subjects were randomized to receive 5 days of EDP-938 600 mg once daily (QD arm) or 500 mg loading dose then 300 mg twice daily (BID arm), or placebo twice daily. Assessments included 12 hourly nasal wash for quantitative RSV viral load, 8 hourly RSV Total Symptom Scoring (TSS) and daily mucus weights. Safety assessments were continued though Day 28 (last follow-up). The primary endpoint was the RSV viral load area under the curve (AUC) from first dose through Day 12 among RSV-infected subjects, defined as the Intent To Treat-Infected (ITT-I) population. The study was fully powered for both RSV viral load and TSS endpoints.

Results. A total of 115 subjects were randomized and inoculated; 86 were included in the ITT-I analysis. The primary and secondary efficacy endpoints were achieved with high statistical significance in QD and BID arms (figure and table). Among EDP-938 recipients all adverse events (AEs) were mild except for a single AE of moderate dyspepsia in the BID arm and events of moderate headache (n = 2) and hypoacusis (n = 1) in the placebo arm. All AEs resolved in follow-up.

Conclusions. In the RSV Challenge study, EDP-938 administered once or twice daily achieved primary and key secondary endpoints with robust reductions in RSV viral load (by both qRT–PCR and plaque assays), symptom scores and mucus weights. These data support the further clinical evaluation of EDP-938 in populations at risk of severe RSV disease.

Endpoint (Mean (±SD))	EDP-938 600 mg QD N=25	EDP-938 500 mg x1 + 300 mg BID N=31	Placebo N=30	P-value EDP-938 vs placebo
AUC by Quantitative RT-PCR (hours x $\log_{10}$ copies/mL)	203.95 (173.50)	217.71 (217.55)	790.15 (408.80)	Both P<0.001
AUC by Plaque Assay (hours x $\log_{10}$ PFU/mL)	34.05 (63.58)	35.91 (78.04)	185.55 (161.71)	Both P<0.001
AUC TSS (hours x Score)	124.47 (115.60)	181.75 (248.42)	478.75 (422.29)	Both P<0.001
Nasal Mucus Weight (grams)	12.965 (13.03)	7.428 (11.13)	33.416 (37.81)	Both P<0.001



Disclosures. Eoin Coakley, MD, Enanta Pharmaceuticals (Employee), Alaa Ahmad, PhD, Enanta Pharmaceuticals (Employee), Kajal Larson, PhD, Enanta Pharmaceuticals (Employee), Ty McClure, PhD, Enanta Pharmaceuticals (Employee), Kai Lin, PhD, Enanta Pharmaceuticals (Employee), Kursten Tenhoor, n/a, Enanta Pharmaceuticals (Consultant), Kingsley Eze, n/a, hVIVO Services Ltd. (Employee), Nicolas Noulin, PhD, No financial relationships or conflicts of interest, Veronika Horvathova, MBChB, MSc, hVIVO Services Limited (Other Financial or Material Support, Employed by hVIVO during the conduct of the study), Bryan Murray, MBBS, No financial relationships or conflicts of interest, Mark Baillet, PhD, S-CUBED (Employee), Julie Mori, PhD, hVIVO (Employee, Shareholder) Nathalie Adda, MD, Enanta Pharmaceuticals (Employee).

LB7. A Randomized, Blinded, Placebo- and Vancomycin-Controlled, First-In-Human (FIH) Study of the Safety, Pharmacokinetics (PK), and Fecal Microbiome Effects of ACX-362E, a Novel Anti-Clostridial DNA Polymerase IIIC (polIIIC) Inhibitor

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