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.

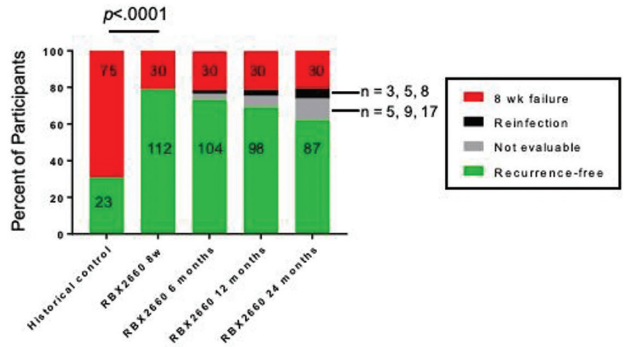

Figure 1: Primary outcome and durability, reported as percentages with number of participants shown as numbers

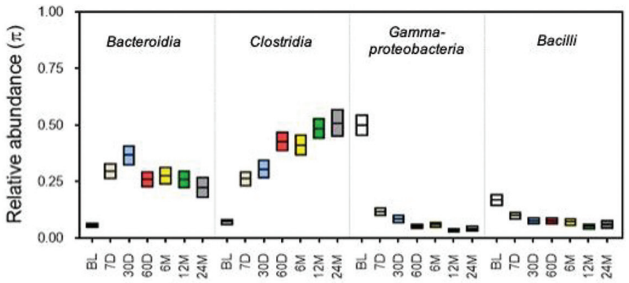

Figure 2: Mean relative abundance (π) with confidence intervals at the taxonomic class level before treatment (BL) and at time points after treatment.

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

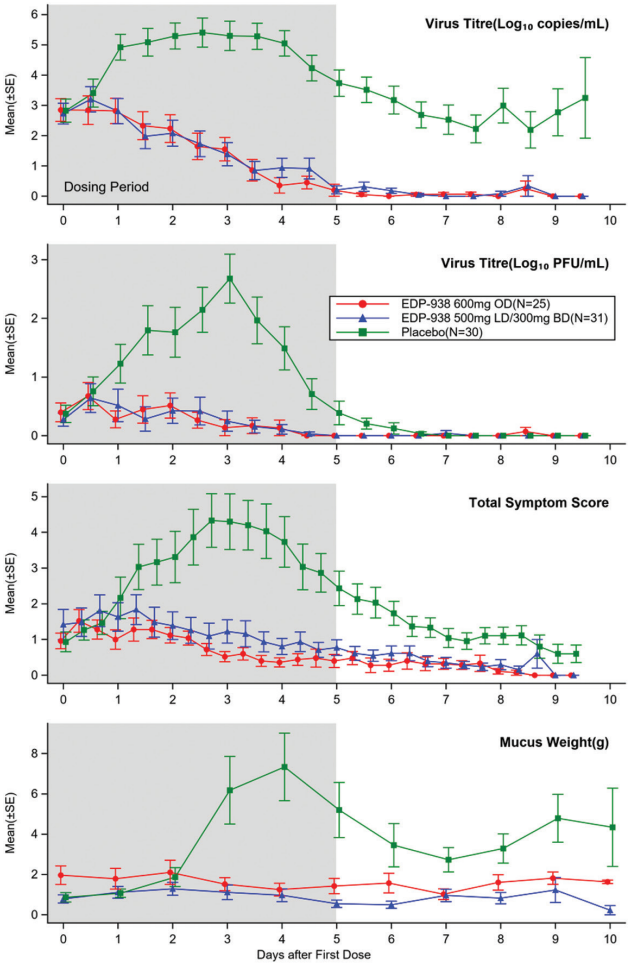
Background. Respiratory syncytial virus (RSV) represents an important global health challenge with significant morbidity and mortality in infants, elderly, and immunocompromised adults. No effective therapy is currently available. EDP-938 demonstrates potent *in vitro* activity against RSV Subtypes A 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

Kevin W. Garey, MS, PharmD[1]; Kevin W. Garey, MS, PharmD[1]; Martin Kankam, MD, PhD, MPH[2]; Julie Mercier, BS[2];

Corinne Seng Yue, BPharm, MSc, PhD[3]; Murray Ducharme, PharmD[3]; Anne J. Gonzales-Luna, PharmD[1]; Anne J. Gonzales-Luna, PharmD[1]; M Jahangir Alam, PhD[1]; Khurshida Begum, PhD[1]; Khurshida Begum, PhD[1]; Michael Silverman, MD[4]; [1]University of Houston College of Pharmacy, Houston, Texas,; [2]Altasciences, Kansas City, Kansas,; [3]Learn and Confirm, Inc., Montreal, Quebec, Canada,; [4]Acurx Pharmaceuticals, LLC, White Plains, New York

Session: 83. Late Breaker Oral Abstract Session 1
Thursday, October 3, 2019: 2:45 PM

Background. ACX-362E, a novel DNA polIIIC inhibitor, is a narrow-spectrum antibacterial selectively active against certain Gram-positive bacteria, including *Clostridioides difficile* (MIC_{90} = 4 µg/mL). The objectives of this phase I study was to assess the safety, pharmacokinetics, and fecal microbiome effects of ACX-362E

Methods. This three-part FIH phase 1, double-blind, randomized healthy volunteer trial determined the safety profile, food effect, and systemic/stool pharmacokinetics of escalating single (150, 300, 600, and 900 mg) and multiple (300 and 450 mg) doses of oral ACX-362E vs. placebo (PBO). Fecal microbiome effects (metagenomic sequencing and qPCR) of multiple-dose ACX-362E were compared with 6 subjects receiving concomitant open-label vancomycin 125 mg four times daily. Dose escalation to each new cohort occurred following review of safety and PK data by a safety oversight committee.

Results. Forty-four subjects received ACX-362E (single dose = 24, multiple doses = 12, food effect = 8) and 12 PBO. Overall, ACX-362E was well tolerated at all dose levels. Adverse events were generally mild and transitory, and no moderate, severe, cumulative, or dose-limiting drug-related adverse events leading to discontinuation were observed. Mean plasma half-life was approximately 2 hours and no accumulation occurred with repeated dosing (Figure 1). Systemic exposure was less than 1 µg/mL and decreased with food. Fecal concentrations during multiple dosing exceeded the *C. difficile* MIC by multiples of up to ~2,500. ACX-362E had minimal effect on Bacteroidetes phylum and caused significantly less dysbiosis than vancomycin (Figure 2).

Conclusion. This FIH clinical trial with ACX-362E demonstrated a favorable safety profile, low systemic and high fecal concentrations, and favorable gut microbiome changes compared with vancomycin. These results shows promise for further clinical development to treat *C. difficile* infections.

Figure 1: **Mean concentration-time profiles - Day 10, linear scale**

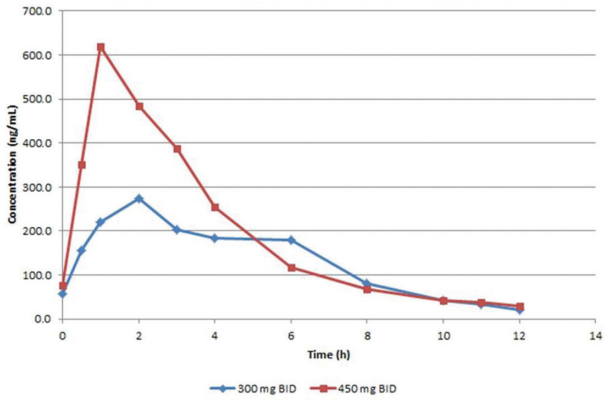
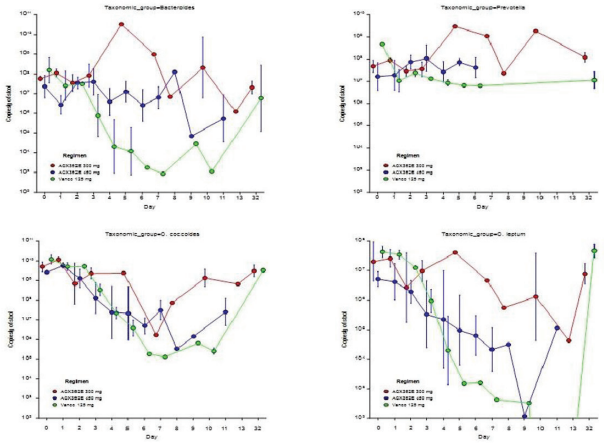


Figure 2. Microbiota levels belonging to different taxonomic groups measured by qPCR in samples



Disclosures. Kevin W. Garey, MS, PharmD, Acurx (Grant/Research Support), Martin Kankam, MD, PhD, MPH, Acurx Pharmaceuticals, LLC (Research Grant or Support), Julie Mercier, BS, Acurx Pharmaceuticals, LLC (Research Grant or Support), Corinne Seng Yue, BPharm, MSc, PhD, Acurx Pharmaceuticals, LLC (Grant/Research Support), Murray Ducharme, PharmD, Acurx Pharmaceuticals, LLC (Grant/Research Support), Anne J. Gonzales-Luna, PharmD, no financial relationships or conflicts of interest, M Jahangir Alam, PhD, No financial relationships or conflicts of interest, Khurshida Begum, PhD, No financial relationships or conflicts of interest, Michael Silverman, MD, Acurx Pharmaceuticals, LLC (Consultant, Employee, Shareholder).

LB8. Microarray Patch Delivery of Long-Acting HIV PrEP and Contraception

Annie Rein-Weston, MPH[1]; Ismaiel Tekko, PhD[2]; Lalit Vora, MPharm, PhD[2]; Courtney Jarrahian, MS[1]; Bill Spreen, PharmD[3]; Trevor Scott, RPh, PhD[3]; Ryan Donnelly, PhD[2]; Darin Zehrung, MBA[1]; [1]PATH, Seattle, Washington,; [2]Queen's University Belfast, Belfast, UK,; [3]ViiV Healthcare, Research Triangle Park, North Carolina

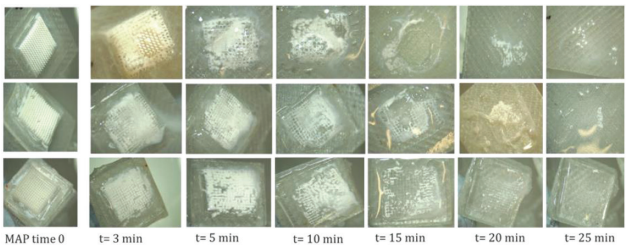
Session: 184. Late Breaker Oral Abstract Session 2
Friday, October 4, 2019: 1:45 PM

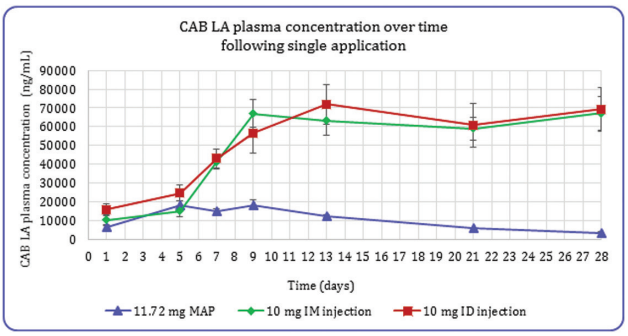
Background. The purpose of this research was to develop a microarray patch (MAP; also known as a microneedle patch) for delivery of long-acting cabotegravir (CAB LA) for HIV pre-exposure prophylaxis (PrEP) and co-delivery of long-acting CAB LA and a hormonal contraceptive to enable a future multi-purpose prevention technology. This abstract presents preclinical pharmacokinetic results of MAP delivery of CAB LA.

Methods. MAPs are an alternative delivery technology in clinical development for intradermal delivery of vaccines and pharmaceuticals. A MAP consists of an array of micron-scale projections (<1 mm in height) amassed on a baseplate and applied to the skin like a bandage. MAPs could provide a discreet delivery system that enables self-administration, which could be particularly important for HIV prevention and contraception for young women and girls in low-resource settings. The purpose of this 3-year, USAID-funded project is to develop a MAP for delivery of long-acting HIV PrEP through to the point of Phase I clinical readiness. Key attributes of the MAP for long-acting HIV PrEP, as defined by our target product profile, include patch size similar to commercially available transdermal patches (20 to 140 cm^2), wear-time of less than 24 hours (ideally 20 minutes), weekly or monthly administration to achieve therapeutic efficacy, and ideally successful self-administration after reading simple product instructions.

Results. We successfully formulated and optimized MAP projection geometry to accommodate high drug-loading requirements of CAB LA (5.86 mg CAB LA per 1 cm^2 MAP), a hydrophobic drug. The MAPs are stable for 6 months under accelerated aging conditions in foil packaging, readily pierce the skin, and rapidly dissolve. In rats, plasma concentration levels of CAB LA were maintained above therapeutic targets of 4xPA-IC90 for 28 days; however, bioavailability was lower than IM or ID injection controls. Photos: QUB. MAPs dissolving over time in phosphate-buffered solution; MAP projections fully dissolved within 25 minutes.

Conclusion. Additional development work is warranted, including optimizing bioavailability, evaluating MAPs as a maintenance dose in vivo, conducting cost of manufacturing and cost of delivery analyses, and assessing potential end-user acceptability.





Disclosures. Bill Spreen, PharmD, ViiV Healthcare (Employee), Trevor Scott, RPh, PhD, ViiV Healthcare (Employee). **Others Authors:** No reported disclosures.

LB9. The Effect of Initiating Integrase Inhibitor-based vs. Non-Nucleoside Reverse Transcriptase Inhibitor-based Antiretroviral Therapy on Progression to Diabetes among North American Persons in HIV Care

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