#	Species of culture	PLG 0206 Dose	CFU Untreated	CFU Treated	Log Reduction
1	*S. epidermidis*	1	1.00E+07	0	7.0
2	*S. epidermidis*	1	1.00E+07	0	7.0
3	*S. aureus* (MSSA)	1	No sonicate*	0	N/A
4	*S. aureus* (MRSA)	0.5	1.00E+07	0	7.0
5	*S. hemolyticus*	1	7.3E+02	0	2.9
6	*E.coli*	1	3.5E+03	60	1.8
	E.coli	1	3.5E+03	30	2.1
	Enterococcus	1	1.40E+04	80	4.1
7	*S. epidermidis*	1	1.90E+04	90	2.3
8	*H. parainfluenzae*	1	1.00E+07	0	7.0
9	*H. parainfluenzae*	1	1.00E+07	0	7.0
10	*S. aureus* (MRSA)	1	1.10E+04	0	4.0

* CFU 1.0E+07 is an estimate of untreated sonicate CFU directly from micro lab measurements.

Table: Summary of culture and CFU log reduction among infected prosthetics exposed and not exposed to PLG0206

Conclusion. Overall, these findings support the ongoing development of PLG0206 as a local irrigation solution at 1 mg/mL concentration in the wound cavity for 15 minutes in patients undergoing treatment of a PJI occurring after total knee arthroplasty.

Disclosures. **David Huang, MD, PhD**, **Peptilogics** (Employee) **Nicholas Pachuda, DPM**, **Peptilogics** (Employee) **Despina Dobbins, BS**, **Peptilogics** (Employee) **Jonathan Steckbeck, PhD**, **Peptilogics** (Employee) **Kenneth Urish, MD, PhD**, **Peptilogics** (Grant/Research Support)

1041. *In vitro* activity of tebipenem against a recent collection of fastidious organisms recovered from respiratory tract infections

S J Ryan Arends, PhD[1]; Abby L. Klauer, n/a[1]; Nicole Cotroneo[2]; Ian A. Critchley, Ph.D.[2]; Rodrigo E. Mendes, PhD[1]; [1]JMI Laboratories, North Liberty, Iowa; [2]Spero Therapeutics

Session: P-59. New Drug Development

Background. Tebipenem is under development as an oral treatment option for complicated urinary tract infections and acute pyelonephritis. This study further evaluated the *in vitro* activity of tebipenem against various fastidious organisms recovered from community-acquired respiratory tract infections (CARTIs).

Methods. The study included a total of 2,476 fastidious organisms: *Haemophilus influenzae* (692 isolates, including fluoroquinolone-resistant, β-lactamase-positive, and β-lactamase-negative ampicillin-resistant [BLNAR]), *Haemophilus parainfluenzae* (30 isolates, including β-lactamase-positive and BLNAR), *Moraxella catarrhalis* (490 isolates), and *Streptococcus pneumoniae* (1,264 isolates, including penicillin-resistant). The isolates were collected primarily from CARTIs (90.8%) and pneumonia in hospitalized patients (PIHPs, 9.2%). Organisms were tested using reference broth microdilution methods in a central laboratory.

Results. Tebipenem had MIC_{90} values of 0.5 mg/L against *H. influenzae* and 1 mg/L against *H. parainfluenzae* isolates. All 18 BLNAR isolates from these two species were inhibited at ≤1 mg/L of tebipenem. The MIC_{90} values observed for ertapenem and meropenem was 0.25 mg/L for these organisms. Tebipenem displayed good activity against *M. catarrhalis* (MIC_{90}, 0.03 mg/L). Tebipenem inhibited 100% of *S. pneumoniae* isolates at ≤1 mg/L. Tebipenem activity (MIC_{90}, 0.12 mg/L) was 8-fold greater than ertapenem (MIC_{90}, 1 mg/L) against *S. pneumoniae* isolates.

Conclusion. Tebipenem displayed potent activity against fastidious organisms causing respiratory tract infections. Greater than 99.7% of all *Haemophilus* isolates, including all BLNAR, were inhibited at ≤1 mg/L. All *M. catarrhalis* isolates were inhibited at ≤0.03 mg/L. Although tebipenem activity correlated with penicillin resistance, all *S. pneumoniae* isolates were inhibited at ≤1 mg/L. Tebipenem *in vitro* activity was greater than ertapenem when tested against *S. pneumoniae* isolates. This data supports the possible development of tebipenem as an oral option for combating CARTIs caused by these organisms.

Table

	Cumulative % at tebipenem MIC of:										
Organism (no. tested)	**≤0.008**	**0.015**	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**MIC_{50}**	**MIC_{90}**
Haemophilus influenzae (692)	8 1.2	21 4.2	71 14.5	184 41.0	200 70.0	117 86.9	72 97.3	17 99.7	2 100.0	0.12	0.5
BLNAR (14)					0 0.0	2 14.3	4 42.9	8 100.0		1	1
Haemophilus parainfluenzae (30)	3 10.0	3 20.0	4 33.3	9 63.3	3 73.3	2 80.0	2 86.7	4 100.0		0.06	1
BLNAR (4)							0 0.0	4 100.0		1	1
Moraxella catarrhalis (490)	11 2.2	232 49.6	247 100							0.03	0.03
Streptococcus pneumoniae (1,264)	911 72.1	28 74.3	50 78.2	133 88.8	80 95.1	59 99.8	2 99.9	1 100.0		≤0.008	0.12
Penicillin-resistant (22; MIC > 4)				0 0.0	6 27.3	15 95.5	1 100.0			0.25	0.25

BLNAR - β-lactamase-negative ampicillin-resistant

Disclosures. **S J Ryan Arends, PhD**, **AbbVie (formerly Allergan)** (Research Grant or Support)**GlaxoSmithKline, LLC** (Research Grant or Support)**Melinta Therapeutics, LLC** (Research Grant or Support)**Nabriva Therapeutics** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support) **Abby L. Klauer, n/a**, **Cidara Therapeutics, Inc.** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support) **Nicole Cotroneo**, **Spero Therapeutics** (Employee, Shareholder) **Ian A. Critchley, Ph.D.**, **Spero Therapeutics** (Employee, Shareholder) **Rodrigo E. Mendes, PhD**, **AbbVie** (Research Grant or Support)**AbbVie (formerly Allergan)** (Research Grant or Support)**Cipla Therapeutics** (Research Grant or Support)**Cipla USA Inc.** (Research Grant or Support)**ContraFect Corporation** (Research Grant or Support)**GlaxoSmithKline, LLC** (Research Grant or Support)**Melinta Therapeutics, Inc.** (Research Grant or Support)**Melinta Therapeutics, LLC** (Research Grant or Support)**Nabriva Therapeutics** (Research Grant or Support)**Pfizer, Inc.** (Research Grant or Support)**Shionogi** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support)

1042. Safety of Investigational Microbiota-Based Live Biotherapeutic RBX2660 in Individuals with Recurrent *Clostridioides difficile* Infection: Data from Five Prospective Clinical Studies

Tricia Braun, PharmD[1]; Beth Guthmueller, AS[2]; Adam J. Harvey, PhD[1]; [1]Rebiotix, A Ferring Company, Roseville, Minnesota; [2]Rebiotix Inc, A Ferring Company, Victoria, Minnesota

Session: P-59. New Drug Development

Background. Microbiota-based treatments have shown promise to reduce recurrence, morbidity, and mortality for recurrent *Clostridioides difficile* infections (rCDI), but consistent and reliable safety data are needed to support regulatory approvals and broaden patient access. Here we provide cumulative safety data from 5 prospective clinical studies evaluating RBX2660—a standardized, microbiota-based investigational live biotherapeutic—for reducing rCDI.

Methods. This analysis included three Phase 2 (PUNCH CD, PUNCH CD2, PUNCH CD Open Label) and two Phase 3 trials (PUNCH CD3, PUNCH CD3-OLS *ad hoc* analysis). Participants were ≥18 years old with documented rCDI who completed standard-of-care oral antibiotic therapy prior to treatment with RBX2660. PUNCH CD3-OLS allowed participants with comorbidities of irritable bowel syndrome (IBS) or inflammatory bowel disease (IBD). Depending on the trial, assigned study treatment was 1 or 2 doses of RBX2660 (or placebo), administered rectally. Participants whose CDI recurred within 8 weeks were eligible for additional RBX2660 treatment. Treatment-emergent adverse events (TEAEs) were recorded for at least 6 months following last study treatment; CD2 and CD Open Label recorded TEAEs for 24 months.

Results. Among 620 participants who received at least one RBX2660 dose (assigned treatment or after recurrence), 324 (52.3%) received 1, 270 (43.5%) received 2, 14 (2.3%) received 3, and 12 (1.9%) received 4. 83 participants received blinded placebo only. A total of 1980 TEAEs were reported from 432 (69.7%) RBX2660-treated participants, compared to 174 TEAEs in 50 (60.2%) placebo-only treated participants. Most TEAEs were mild or moderate in severity, with diarrhea common in all treatment groups. No potentially life-threatening TEAEs were considered related to RBX2660. Study discontinuation due to TEAEs was minimal (< 1%) with none related to RBX2660. There were no reported infections for which the causative pathogen was traced to RBX2660.

Conclusion. Across five clinical studies with consistent investigational product, RBX2660 was well-tolerated in rCDI participants. In aggregate, this data provides compelling and consistent safety data for RBX2660.

Disclosures. **Tricia Braun, PharmD**, **Rebiotix, a Ferring Company** (Employee) **Beth Guthmueller, AS**, **Rebiotix Inc, A Ferring Company** (Employee) **Adam J. Harvey, PhD**, **Rebiotix, A Ferring Company** (Employee)

1043. Activity of Mecillinam Against Enterobacterales Isolates Collected From Patients With Urinary Tract Infections (UTIs) in the USA During 2019

Stephen Hawser, PhD[1]; Ian Morrissey[2]; Anne Santerre Henriksen, MS[3]; [1]IHMA, Monthey, Valais, Switzerland; [2]IHMA Europe, Monthey, Valais, Switzerland; [3]Maxel Consulting ApS, London, England, United Kingdom

Session: P-59. New Drug Development

Background. Mecillinam is a β-lactam antibiotic that exerts its antibacterial activity by binding to penicillin-binding protein 2. In the USA, intravenous (IV) mecillinam is in development for the treatment of complicated UTIs in the hospital setting and as step-down therapy transitioning from IV mecillinam to oral pivmecillinam so that patients can continue treatment at home. To support the clinical development of mecillinam in the USA for the treatment of both complicated and uncomplicated UTI, this observational study investigated the activity of mecillinam against Enterobacterales isolates from patients with UTI in the USA, collected during 2019.

Methods. This study evaluated the activity of mecillinam and other antimicrobial agents against 1075 selected Enterobacterales clinical isolates collected from patients with UTI in the USA during 2019. Antibiotic activity (minimum inhibitory concentration [MIC]) was determined by Clinical & Laboratory Standards Institute (CLSI) agar dilution methodology, and susceptibility was interpreted according to CLSI guidelines.

Results. Among the selected 1075 isolates, producers of extended-spectrum beta-lactamase (ESBL) represented 9.6% of *Escherichia coli* and 50% of *Klebsiella pneumoniae*. Ninety-five percent of the isolates tested were susceptible to mecillinam (Table 1). The MIC_{50} and MIC_{90} values for mecillinam were 0.25 and 2 μg/mL, respectively. Fosfomycin MIC_{50} and MIC_{90} were 1 and 32 μg/mL, respectively (97.6% of isolates

were susceptible). Mecillinam showed the lowest MIC_{90} value of all single antibiotics tested. The highest MIC_{90} was 128 µg/mL for both nitrofurantoin and cefotaxime. The lowest percentage of resistance was obtained with fosfomycin (1.7%), followed by mecillinam (4%).

Table 1: Summary MIC and susceptibility data for all isolates tested (n=1075)

	MIC (µg/mL)				CLSI susceptibility			
Drug	MIC 50	MIC 90	MIN	MAX	Breakpoints (S|I|R)	%S	%I	%R
CTZ	>64	>64	≤0.25	>64	≤1 | 2 | ≥4	32.4	1.1	66.5
CTZ/CLAV [4 µg/mL]	≤0.25	1	≤0.25	32	No Breakpoints Defined	-	-	-
CTX	16	128	≤0.25	>128	≤4 | 8 | ≥16	37.4	7.1	55.5
CTX/CLAV [4 µg/mL]	≤0.25	2	≤0.25	64	No Breakpoints Defined	-	-	-
CRO	0.03	>8	≤0.015	>8	≤1 | 2 | ≥4	81.4	0.6	18.1
CIP	0.015	>8	≤0.002	>8	≤0.25 | 0.5 | ≥1	77.4	2.1	20.6
FOS	1	32	0.25	>256	≤64 | 128 | ≥256	97.6	0.7	1.7
MEC*	0.25	2	≤0.015	>128	≤8 | 16 | ≥32	95.0	1.0	4.0
NIT	16	128	≤2	>128	≤32 | 64 | ≥128	69.6	14.5	15.9
SXT (1:19)	0.12	>8	≤0.015	>8	≤2/38 | – | ≥4/76	73.8	-	26.2

*Using CLSI breakpoints for *E. coli*
CLSI: Clinical & Laboratory Standards Institute; CTZ: ceftazidime; CTZ/CLAV: ceftazidime/clavulanate; CTX: cefotaxime; CTX/CLAV: cefotaxime/clavulanate; CRO: ceftriaxone; CIP: ciprofloxacin; FOS: fosfomycin; I: intermediate; MEC: mecillinam; MIC: minimum inhibitory concentration; NIT: nitrofurantoin; R: resistance; S: susceptibility; SXT: trimethoprim/sulfamethoxazole

Conclusion. Overall, mecillinam showed excellent activity and a comparable resistance profile to fosfomycin. Resistance rates to ceftazidime, cefotaxime, ciprofloxacin and trimethoprim/sulfamethoxazole of greater than 20% are concerning due to the frequent use of these antibiotics in clinical practice to treat UTIs. Taken together, these data demonstrate that mecillinam has promising activity, with low resistance observed in Enterobacterales species causing UTIs in the USA. Clinical development of mecillinam in the USA is ongoing.

Disclosures. **Stephen Hawser, PhD**, **Utility Therapeutics** (Grant/Research Support) **Ian Morrissey**, **Utility Therapeutics** (Grant/Research Support) **Anne Santerre Henriksen, MS**, **Advanz** (Consultant)**Shionogi BV** (Consultant)**UTILITY Therapeutics** (Consultant)

1044. *In vitro* Activity of Tebipenem Against Relevant Clinical Isolates in the Presence of Pulmonary Surfactant

S J Ryan Arends, PhD[1]; Abby L. Klauer, n/a[1]; Nicole Cotroneo[2]; Ian A. Critchley, Ph.D.[2]; Rodrigo E. Mendes, PhD[1]; [1]JMI Laboratories, North Liberty, Iowa; [2]Spero Therapeutics

Session: P-59. New Drug Development

Background. Tebipenem (TBP) is an orally administered broad-spectrum carbapenem antibiotic under development for the treatment of acute pyelonephritis and complicated urinary tract infections. This study evaluated the effect of bovine pulmonary surfactant (BPS) on the *in vitro* activity of TBP and ertapenem (ETP) against a recent collection of clinical isolates.

Methods. A total of 10 isolates recovered from patients with infections in 2018 were tested for antimicrobial susceptibility to TBP and ETP in the absence or presence of 1%, 5%, or 10% BPS (Infasurf; ONY Biotech). These isolates included the following species: *C. freundii*, *E. cloacae*, *E. coli*, *H. influenzae*, *H. parainfluenzae*, *K. pneumoniae*, methicillin-susceptible *S. aureus*, *M. catarrhalis*, *S. pneumoniae*, and *S. pyogenes*. Isolates were tested with the appropriate broth microdilution method for each organism as specified by CLSI. For most organisms, MICs were determined in cation-adjusted Mueller-Hinton broth (CAMHB). CAMHB was supplemented with 2.5-5% lysed horse blood for streptococci and *Haemophilus* Test Medium broth for *Haemophilus* spp. Daptomycin (DAP) was tested against *S. aureus* ATCC 29213 as a positive control.

Results. All isolates displayed TBP MIC values ranging from ≤0.004 to 0.06 mg/L in media without BPS. There were no observed MIC increases >2-fold in the presence of BPS. 4 of the 10 isolates displayed slightly higher (≥4-fold) ETP than TBP MIC values. The ETP MIC values ranged from 0.015-0.25 mg/L in media without BPS. Similarly, there were no observed instances of a >2-fold shift toward lower potency in the presence of BPS. For both TBP and ETP, MIC endpoint values were easily determined, except for in the case of the 2 *Haemophilus* strains growing in the presence of 5% or 10% BPS. For these conditions, resazurin was added to establish an MIC value. The MIC values found with this method did not differ from the MIC values found in either HTM media or HTM media with 1% BPS. As expected, the addition of BPS shifted DAP *S. aureus* MIC values to >8 mg/L for all 3 BPS concentrations.

Conclusion. TBP displayed potent activity against all isolates tested, as all observed MIC values were ≤0.06 mg/L. The addition of BPS to the testing medium did not affect the *in vitro* MIC values of TBP or ETP against these species.

Disclosures. **S J Ryan Arends, PhD**, **AbbVie (formerly Allergan)** (Research Grant or Support)**GlaxoSmithKline, LLC** (Research Grant or Support)**Melinta Therapeutics, LLC** (Research Grant or Support)**Nabriva Therapeutics** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support) **Abby L. Klauer, n/a**, **Cidara Therapeutics, Inc.** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support) **Nicole Cotroneo**, **Spero Therapeutics** (Employee, Shareholder) **Ian A. Critchley, Ph.D.**, **Spero Therapeutics** (Employee, Shareholder) **Rodrigo E. Mendes, PhD**, **AbbVie** (Research Grant or Support)**AbbVie (formerly Allergan)** (Research Grant or Support)**Cipla Therapeutics** (Research Grant or Support)**Cipla USA Inc.** (Research Grant or Support)**ContraFect Corporation** (Research Grant or Support)**GlaxoSmithKline, LLC** (Research Grant or Support)**Melinta Therapeutics, Inc.** (Research Grant or Support)**Melinta Therapeutics, LLC** (Research Grant or Support)**Nabriva Therapeutics** (Research Grant or Support)**Pfizer, Inc.** (Research Grant or Support)**Shionogi** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support)

1045. Safety of the Synthetic Saponin Adjuvant TQL1055: Preliminary Results from a First-in-humans Trial

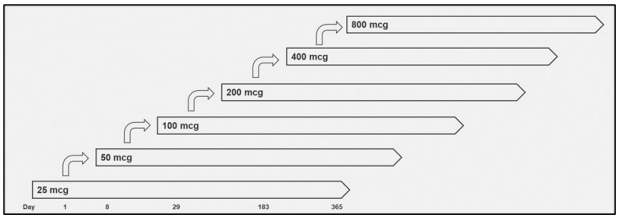
Sean R. Bennett, MD PhD[1]; Tyler Martin, MD[2]; [1]Adjuvance Technologies, Inc., Lincoln, Nebraska; [2]Adjuvance Technologies, Lincoln, Nebraska

Session: P-60. New Vaccines

Background. Saponin adjuvants reliably enhance immune response to a variety of antigens, but their use is hindered by dose-limiting toxicities and supply constraints. TQL1055 is a semi-synthetic analog of the natural saponin adjuvant QS-21, rationally modified to improve tolerability and enable large-scale manufacturing. We previously showed that the combination of acellular pertussis vaccine (aP) and TQL1055 was well-tolerated and increased anti-pertussis toxin (PT) antibody responses in mice and rabbits, with a no observed adverse effect level (NOAEL) > 2000 mcg/dose.

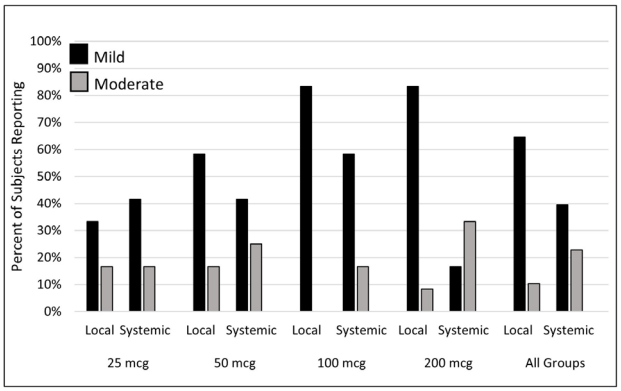
Methods. Here we report interim results from a Phase 1 first-in-humans dose-escalation study of TQL1055. Healthy adults 18 to 50 years of age were sequentially enrolled into 6 groups (n=12/group) and randomized 10:2 to receive one intramuscular dose of aP + TQL1055 or aP alone on Day 1. TQL1055 dose increased by group from 25 to 800 mcg (Figure 1). Local adverse events (AEs) (injection site pain, redness, swelling) and systemic AEs (fever, chills, headache, fatigue, myalgia, arthralgia, nausea, vomiting, diarrhea) were solicited through Day 8. Clinical laboratory panels (chemistry, hematology, coagulation) were performed on Days 1 (pre-dose), 8, and 29. Serious AEs were collected through Day 365. Antibodies to PT were assessed at all visits.

Figure 1. Study Design



Results. Blinded safety data from the first four groups (n=48) through Day 8 were analyzed, including 2 subjects/group receiving aP alone. All solicited AEs were mild or moderate (Figure 2). Local AEs, mainly injection site pain, occurred in 75% of subjects (mild 65%, moderate 10%). The incidence of total local AEs increased with TQL1055 dose, from 50% at 25 mcg to 92% at 200 mcg. The mean duration of local AEs was 1.8 days and also increased with TQL1055 dose, from 1.3 days at 25 mcg to 2.1 days at 200 mcg. Systemic AEs, mostly fatigue, headache, and nausea, occurred in 63% of subjects (mild 40%, moderate 23%), with no fevers. The mean duration of systemic AEs was 1.4 days, with no association with TQL1055 dose. No severe or serious adverse events were reported.

Figure 2. Solicited Adverse Events by Severity and TQL1055 Dose



Conclusion. In this early analysis, the safety profile of aP + TQL1055 appears similar to that of licensed aP vaccines, without severe or prolonged injection site pain. These data support further dose escalation and assessment of immunogenicity.

Disclosures. **Sean R. Bennett, MD PhD**, **Adjuvance Technologies** (Employee) **Tyler Martin, MD**, **Adjuvance Technologies** (Employee, Shareholder)

1046. Immunogenicity and Safety of a Quadrivalent Meningococcal Conjugate Vaccine (MenACYW-TT) Administered as a Booster to Adults ≥ 59 Years of Age

Corwin A. Robertson, MD, MPH, FACP[1]; Jeffry Jacqmein, MD[2]; Alexandre Selmani, PhD[1]; Katherine Galarza, MD[1]; Philipp Oster, MD[1]; [1]Sanofi Pasteur, Swiftwater, Pennsylvania; [2]University of Florida Health Family Medicine, Jacksonville, Florida