ContraFect

MOLECULAR TREATMENTS
FOR INFECTIOUS DISEASE

Corporate Presentation

May 2022

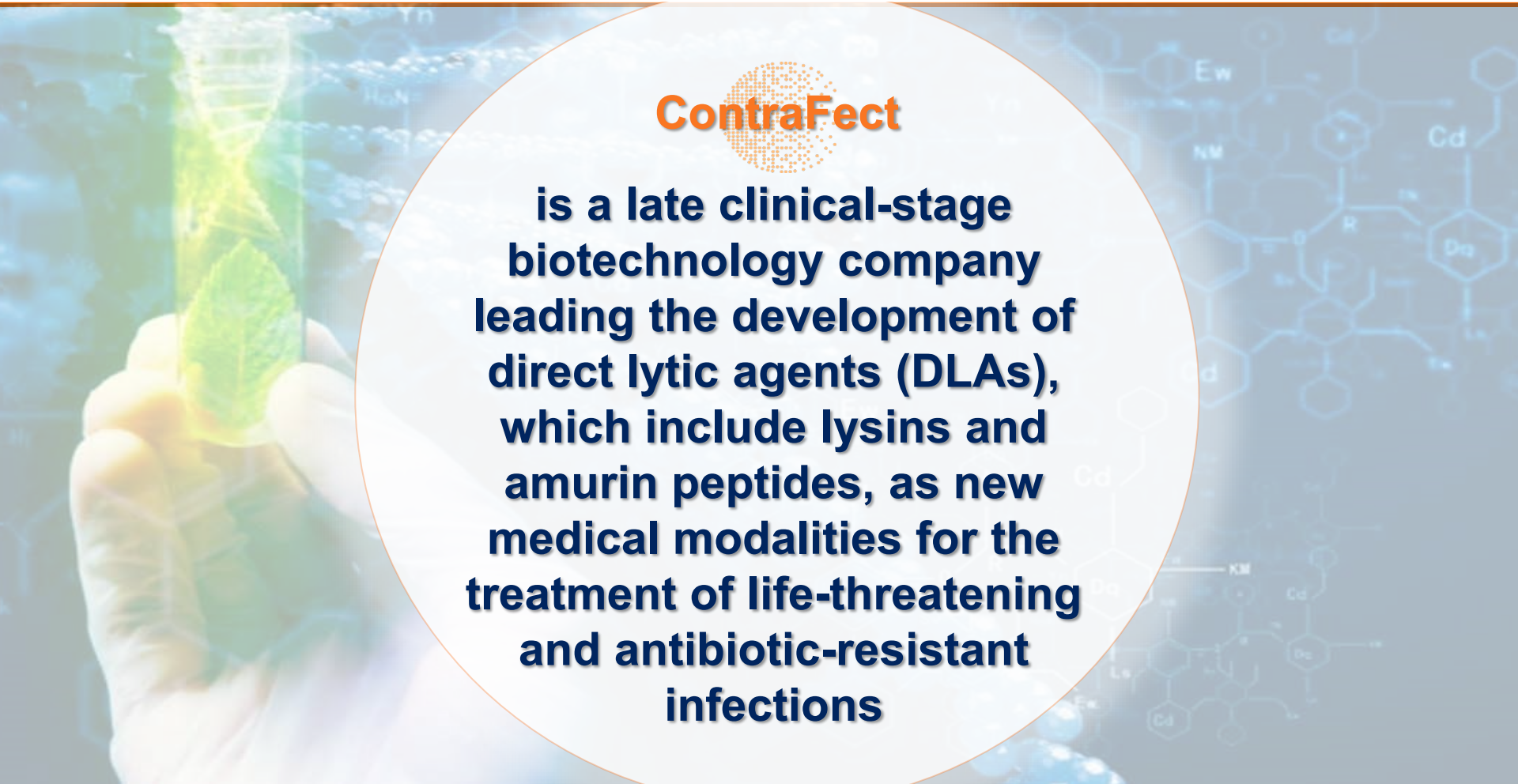
NASDAQ: CFRX

Forward Looking Statements

ContraFect

This presentation contains, and our officers and representatives may from time to time make, "forward-looking statements" within the meaning of the U.S. federal securities laws. Forward-looking statements can be identified by words such as "projects," "may," "will," "could," "would," "should," "believe," "expect," "target", "anticipate," "estimate," "intend," "plan," "proposed", "potential" or similar references to future periods. Examples of forward-looking statements in this presentation include, without limitation, statements made regarding ContraFect Corporation's ("ContraFect") ability to develop DLAs as new medical modalities for the treatment of life-threatening, antibiotic-resistant infections, cited information, ContraFect's End-of Phase 2 meeting with the FDA, Phase 3 plans, designs and timing, Phase 2 study results, data analyses and comparisons, health economic data, safety and efficacy of exebacase, exebacase's value proposition, patent protection, commercial assessments, *in vitro* and *in vivo* study results, ContraFect's plans regarding its next IND and extrapolated data. Forward-looking statements are statements that are not historical facts, nor assurances of future performance. Instead, they are based on ContraFect's current beliefs, expectations and assumptions regarding the future of its business, future plans, proposals, strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent risks, uncertainties and changes in circumstances that are difficult to predict and many of which are beyond ContraFect's control, including those detailed in ContraFect's Quarterly Report on Form 10-Q for the period ended March 31, 2022, and other filings with the Securities and Exchange Commission ("SEC"). Actual results may differ from those set forth in the forward-looking statements. Important factors that could cause actual results to differ include, among others, the occurrence of any adverse events related to the discovery, development and commercialization of ContraFect's product candidates such as unfavorable clinical trial results, insufficient supplies of drug products, the lack of regulatory approval, or the unsuccessful attainment or maintenance of patent protection. Any forward-looking statement made by ContraFect in this presentation is based only on information currently available and speaks only as of the date on which it is made. No representation or warranty is made as to the completeness or accuracy of the information provided in this presentation. Except as required by applicable law, ContraFect expressly disclaims any obligations to publicly update any forward-looking statements, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise. Audiences are cautioned that forward-looking statements or similar information are not guarantees of future performance and, accordingly, are expressly cautioned not to put undue reliance on forward-looking statements or similar information due to the inherent uncertainty therein.

About ContraFect



ContraFect

is a late clinical-stage biotechnology company leading the development of direct lytic agents (DLAs), which include lysins and amurin peptides, as new medical modalities for the treatment of life-threatening and antibiotic-resistant infections

Senior Leadership

Roger Pomerantz, MD, FACP – CEO

SERES THERAPEUTICS · MERCK · Johnson & Johnson · tibotec

Cara Cassino, MD, FCCP – CMO & EVP, R&D

Forest Laboratories, Inc. · Pfizer · Boehringer Ingelheim

Michael Messinger – CFO

Lexicon pharmaceuticals · EY

Natalie Bogdanos – GC, Secretary & DPO

Enzo

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Formerly at Lazard, JP Morgan, Lehman

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EVP & CCO, Real Endpoints
Former Associate CMO, CVS Health
Former VP, Clinical Innovation, Medco

Michael Otto, PhD

Former CSO,
Pharmasset

Steven C. Gilman, PhD – Vice Chair

Former CEO, ContraFect

Former EVP, R&D and CSO, Cubist

Cary Sucoff

President,
Equity Source Partners

The Burden of Bacterial Antimicrobial Resistance

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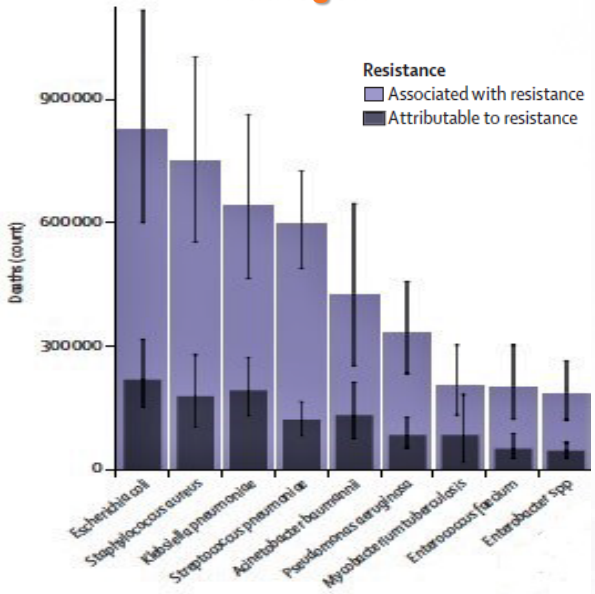
There remains an urgent need for alternatives that will circumvent bacterial resistance to current medicines

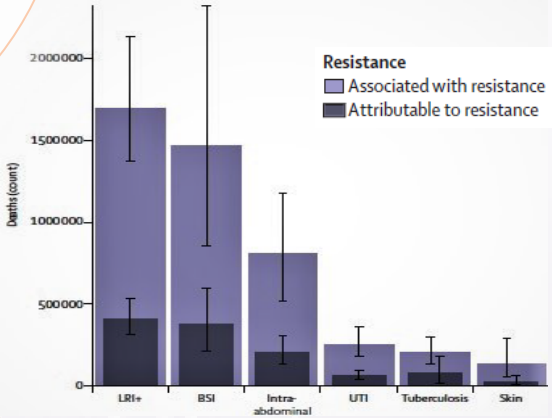
Exebacase is the only agent in Phase 3 with a novel target

Antibacterial innovation stems from small, emerging biotechnology companies

Deaths by Resistant Pathogen



Deaths by Infection Type



Sources: (1) The State of Innovation in Antibacterial Therapeutics, Bio, February 2022, excluding agents for *C. difficile*
(2) Global burden of bacterial antimicrobial resistance in 2019:a systematic analysis, Lancet, January 2022

Medical Paradigm Shifts in Standard-of-Care

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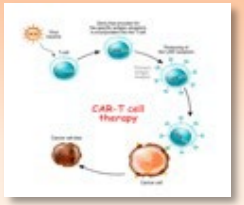
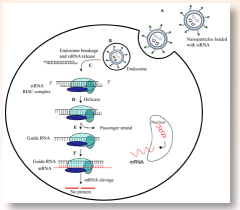
	PRIOR TREATMENT		NEW TREATMENT	
Anti-Infectives	 Antibiotics	Superiority Mortality benefits Positive health economics	Microbiome Direct lytic agents	
Cancer	 Chemotherapy		Immunotherapies	
Congenital Disorders	No treatments available		Gene therapies	

Product Candidate Portfolio in Perspective

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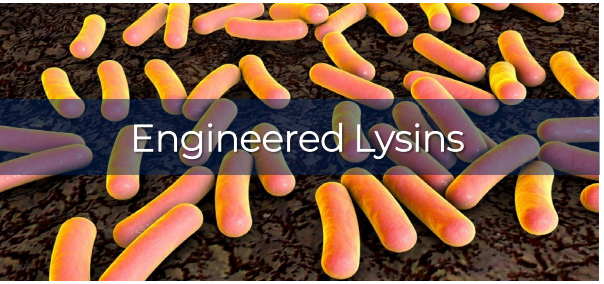
LEADING THE DEVELOPMENT OF DLAs AS NEW MEDICAL MODALITIES



We have engineered lysins which permeate the outer membrane and kill Gram-negative pathogens, including multi-drug resistant (MDR) strains.

CF-370, targeting Gram-negative pathogens, including drug-resistant *Pseudomonas aeruginosa*

- Expect to file an IND application in 2022

Ongoing Phase 3 superiority study comparing to standard-of-care antibiotics alone

- Interim futility analysis expected in July 2022
- Expect complete enrollment by end of 2022

Only Phase 3 antibacterial agent with a novel target(1)

Substantial clinical benefit observed in MRSA patients in Phase 2b superiority trial

Breakthrough Therapy and Fast Track designations and Streamlined Development from FDA

First investigational non-antibiotic anti-infective developed in the US

We have discovered a new class of antimicrobial peptides for which we have observed potent activity across a broad range of resistant Gram-negative ESKAPE pathogens

Source: (1) The State of Innovation in Antibacterial Therapeutics, Bio, February 2022, excluding agents for *C. difficile*

ContraFect Portfolio

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Program *Pathogen*	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Launch
Exebacase *Staphylococcus aureus*	Bacteremia, including endocarditis — *Fast Track* — *Breakthrough Therapy*					
	Prosthetic joint infections (PJI) — *Compassionate Use*					
	MRSA bacteremia in COVID patients — *Expanded Access*					
CF-296 *Staphylococcus aureus*	Osteomyelitis and PJI					
CF-370 *Pseudomonas aeruginosa*	IND enabling activities					
Amurins *Broad spectrum Gram-negative ESKAPE pathogens*						
Gram-negative lysins *Klebsiella pneumoniae Escherichia coli Enterobacter cloacae Acinetobacter baumannii*						

BARDA

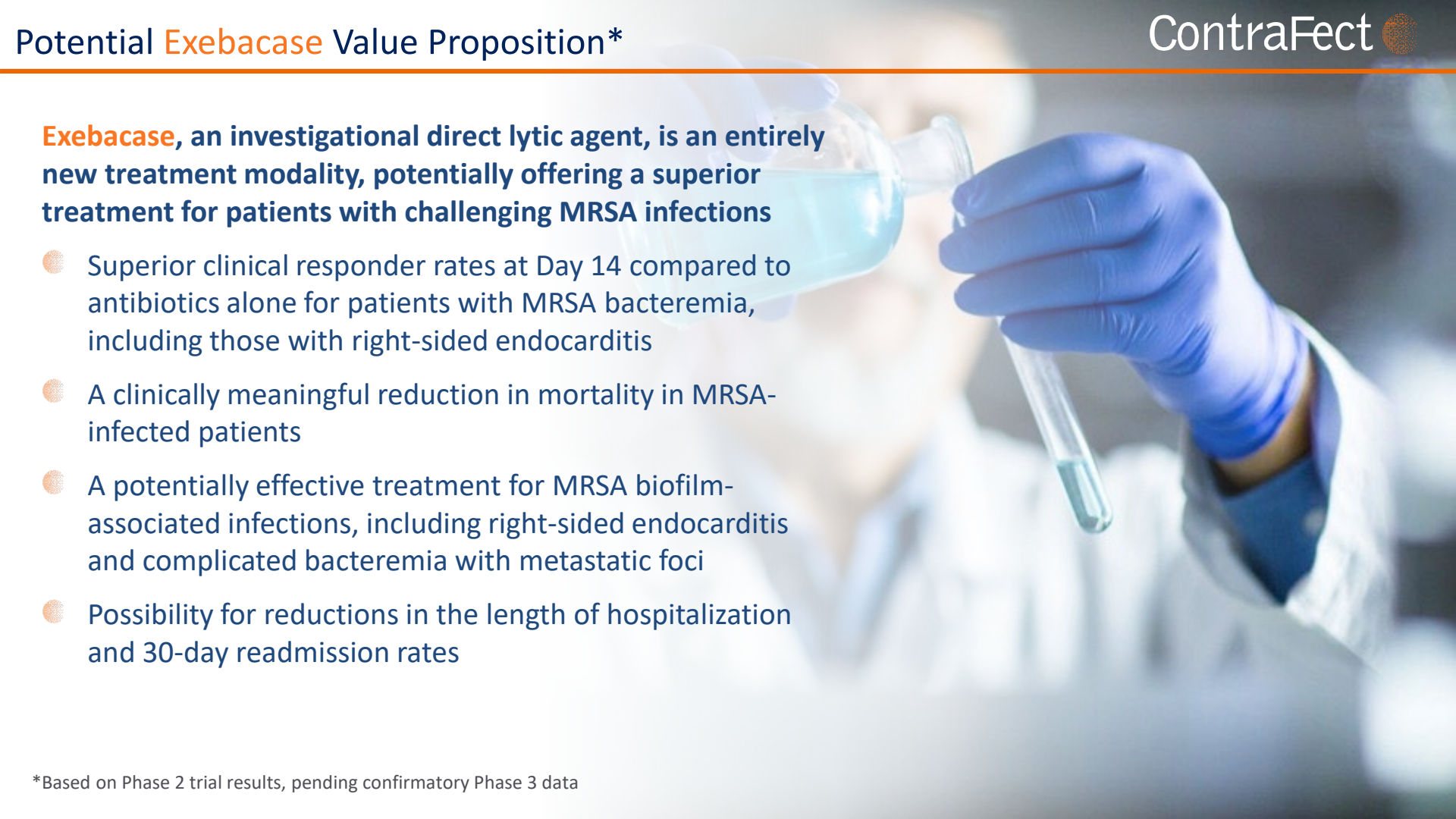
Exebacase (CF-301)

Novel, First-In-Class, Direct Lytic Agent for *Staph aureus* Bacteremia, Including Right-Sided Endocarditis

Potential Exebacase Value Proposition*

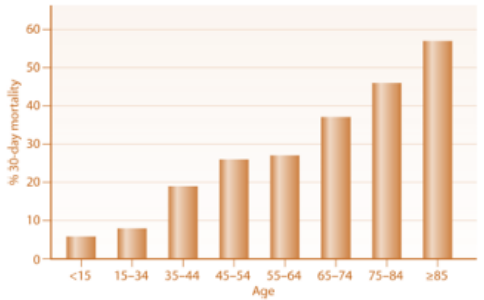
Exebacase, an investigational direct lytic agent, is an entirely new treatment modality, potentially offering a superior treatment for patients with challenging MRSA infections

- Superior clinical responder rates at Day 14 compared to antibiotics alone for patients with MRSA bacteremia, including those with right-sided endocarditis
- A clinically meaningful reduction in mortality in MRSA-infected patients
- A potentially effective treatment for MRSA biofilm-associated infections, including right-sided endocarditis and complicated bacteremia with metastatic foci
- Possibility for reductions in the length of hospitalization and 30-day readmission rates



*Based on Phase 2 trial results, pending confirmatory Phase 3 data

History of Treatments for Methicillin-Resistant Staph aureus (MRSA) Bacteremia



Sources: (1) Extracted from Predictors of Mortality in *Staphylococcus aureus* Bacteremia, van Hal, 2012
(2) Referenced in *Staphylococcus aureus* Infections: Epidemiology, Pathophysiology, Clinical Manifestations and Management, Tong, 2015

Staph aureus Bacteremia, Particularly MRSA, is Worsening

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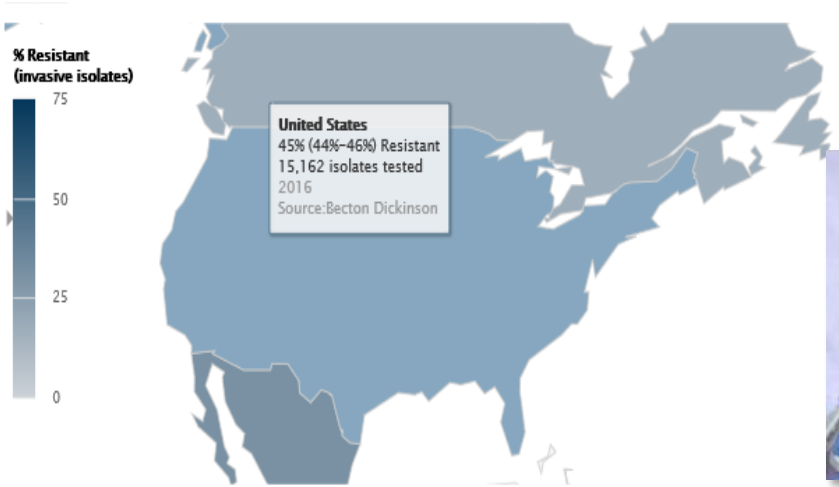
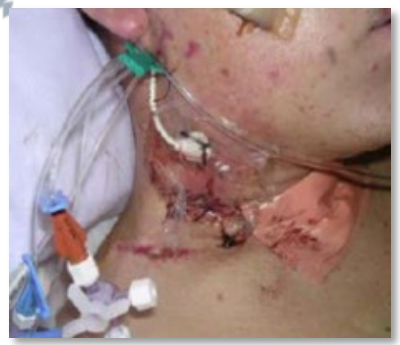
21-Year, Prospective, Longitudinal Study of Staph aureus Bacteremia[2]

- Increasing disease severity
- Increased rates of USA300 (MRSA) strain
- Increase in metastatic infections from USA300
- Patients have increasing number of comorbidities

1995



2016



Sources: (1) Extracted from The Center for Disease Dynamics, Economics & Policy website
(2) Changing Characteristics of Staphylococcus aureus Bacteremia: Results From a 21-Year, Prospective, Longitudinal Study, Souli, 2019

Exebacase: First-in-Class Lysin Candidate

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Key attributes

- 26 kDa modular bacterial cell wall hydrolase enzyme
- Highly potent against *Staph aureus* and unique lysis and eradication of *Staph* biofilms
- Potent synergy with broad range of anti-staphylococcal antibiotics

Clinical-stage program

- Advancing with FDA Breakthrough Therapy designation and under guidance for Streamlined Development for antibacterial therapies
- Ongoing Phase 3 DISRUPT superiority trial
- Completed Phase 2 superiority study with positive results
  - Significant improvement in MRSA patient responder rates with over 40% increase over standard-of-care antibiotics alone, 74.1% vs. SOC 31.3% (p=0.010)
  - Demonstrated favorable safety and tolerability data in patients

Broad patent protection

- Patent with composition of matter claims expiring in 2032
- Patents with method claims for killing all Staph strains expiring in 2032 and method claims for treatment of Staph strain biofilms expiring in 2033

The DISRUPT (Direct Lysis of Staph aureus Resistant Pathogen Trial) Study

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Single, pivotal Phase 3 trial – The path to potential registration

- Randomized, double-blind, placebo-controlled
- Compares efficacy of single IV dose of exebacase plus standard-of-care antibiotics to standard-of-care antibiotics alone
- Study population includes patients with *Staph aureus* bacteremia, including right-sided endocarditis (left-sided endocarditis is excluded)
- Number of subjects: ~350 patients randomized 2:1 (exebacase:placebo)
- Conducted in the US Only
- **Primary efficacy endpoint**: Clinical response at Day 14 in patients with **MRSA** bacteremia, including right-sided endocarditis
  - Interim futility analysis at 60% of enrollment expected in July 2022

Additional Study Design Elements of the DISRUPT Study

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- Secondary and exploratory endpoints:
  - 30-day all-cause mortality in MRSA patients
  - Clinical response at Day 14 in All Staph aureus patients
  - Clinical response at Day 30 and Day 60
- Evaluation of impact on health resource utilization:
  - Length of time in ICU and of hospital stay
  - 30-day readmission rates
- Statistical Parameters:

	Primary Efficacy Endpoint: Clinical Response at Day 14 (MRSA Patients)	Secondary Efficacy Endpoint: Mortality (MRSA Patients)	Secondary Efficacy Endpoint: Clinical Response at Day 14 (All Staph aureus Patients)
Target difference	28% increase over SOC Antibiotics	17% decrease over SOC antibiotics alone	16% increase from SOC antibiotics alone
Power	86%	80%	83%

Phase 3 Based on Phase 2 Design

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Primary endpoint – Clinical response at Day 14

- Determined by independent, blinded Adjudication Committee
- Defined as “improvement/resolution of signs/symptoms, no new metastatic foci of infection or complications, and no changes in antibiotic treatment or further medical intervention due to lack of response in patients alive at time of evaluation”

Primary analysis group

- 116 patients with confirmed *Staph aureus* bacteremia/endocarditis who received study drug (79% enrolled in the US)
- Approximately one-third of patients had methicillin-resistant staph aureus (MRSA) and two-thirds of patients had methicillin-sensitive *Staph aureus* (MSSA)
- Antibiotic treatment with vancomycin or daptomycin for MRSA and semi-synthetic penicillins or first generation cephalosporins for MSSA was similar in treatment arms

Pre-specified subgroups

- MRSA
- Bacteremia including right-sided endocarditis

Overview of Phase 2 Results Based on Phase 3 Design

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Primary endpoint – Clinical response at Day 14

- In defined Phase 3 primary efficacy population of **MRSA** bacteremia patients
  82.6% response vs. 33.3% SOC alone (p=0.005)

Secondary endpoint – 30-Day all-cause mortality

- In defined Phase 3 population of **MRSA** bacteremia patients
  4.4% mortality vs. 20.0% on SOC alone

Secondary endpoint – Clinical response at Day 14

- In defined Phase 3 secondary efficacy population of **All *Staph aureus*** bacteremia patients
  83.7% response vs. 54.3% SOC alone (p=0.006)

Other endpoints – Health economics

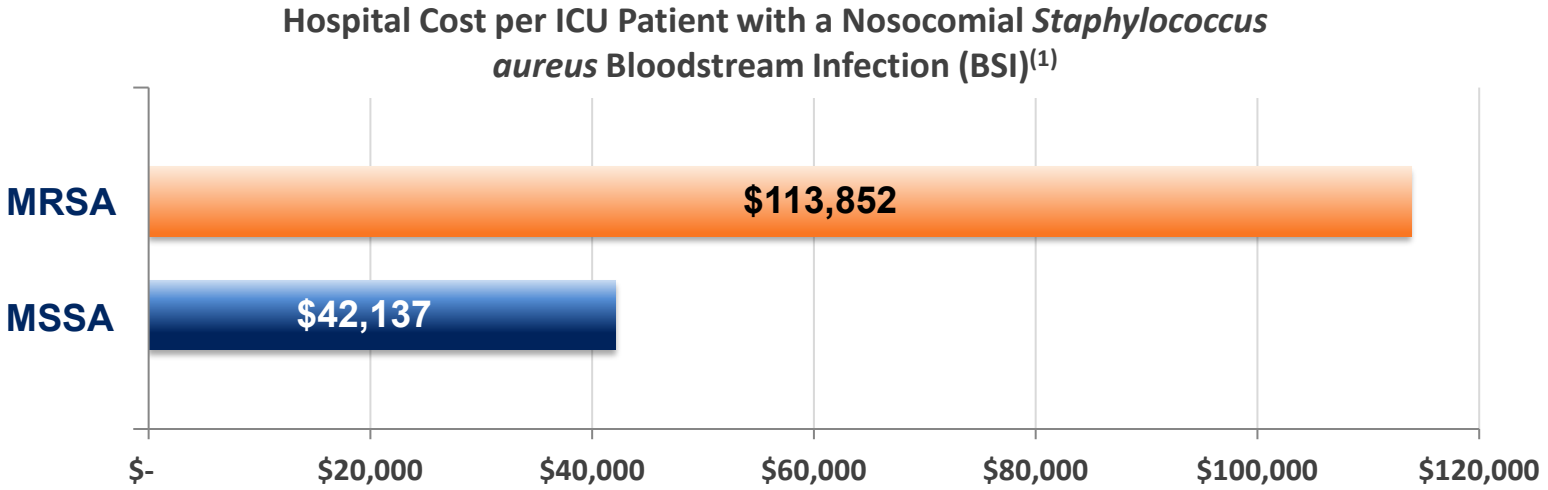
- Reduced length of hospital stay for **MRSA** patients
  6.0 days vs. 10 days on SOC alone
- Reduced 30-day hospital readmission rates among **MRSA** patients
  for all-causes, rate of 13.0% vs. 30.8% on SOC alone
  for Staph, rate of 4.3% vs. 15.5% on SOC alone

Well-tolerated through Day 180

- Similar tolerability to SOC alone
- **No SAEs determined to be related to exebacase**

MRSA Bacteremia Opportunity for First-Line Commercial Impact

Exebacase, for the treatment of Staphylococcus aureus bloodstream infections (bacteremia), including those with right-sided infective endocarditis, when used in addition to standard-of-care anti-staphylococcal antibiotics, in adult patients



MRSA surgical site and central line-associated bloodstream infections were found to increase length of stay the most (up to 23 days) and be the highest cost (up to $175,000)(2)

Sources: (1) Ben-David, Infection Control and Hospital Epidemiology, May 2009, Vol. 30, No. 5, pp. 453-460; (2) Zimlichman, JAMA Internal Medicine, September 2, 2013

Transition From Compassionate Use to Evaluate Exebacase in PJI Study

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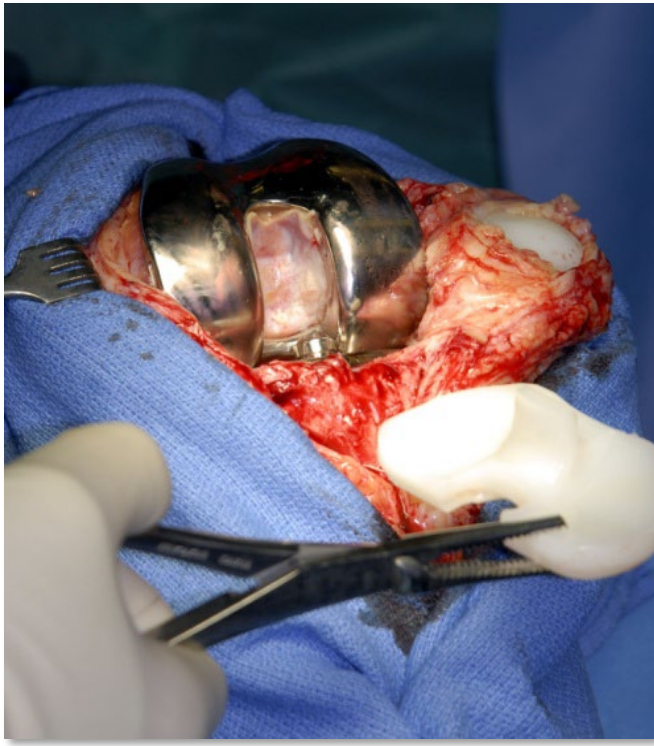
Prosthetic joint infections (PJI)[1]

- Annual estimated cost to US hospitals of over $1.8B in 2030[1]
- Estimated 40,000 infections from knee procedures and 25,000 infections from hip procedures in US by 2030 with 2-3% infection rate[1]
- Risk of infection up to 50% in patients with a wide range of comorbidities[2][3]
  - history of previous surgery
  - poorly controlled diabetes
  - morbid obesity
  - chronic renal disease
  - active liver disease
  - excessive smoking or alcohol consumption
  - intravenous drug abuse



Sources: (1) Premkumar et al., Projected Economic Burden of Periprosthetic Joint Infection in the United States. Journal of Arthroplasty, 2020
(2) Proceedings of the International Consensus Meeting on Periprosthetic Joint Infection, 2019
(3) Serrier et al., Economic study of 2-stage exchange in patients with knee or hip prosthetic joint infection. Frontiers, 2020

Transition From Compassionate Use to Evaluate Exebacase in PJI Study

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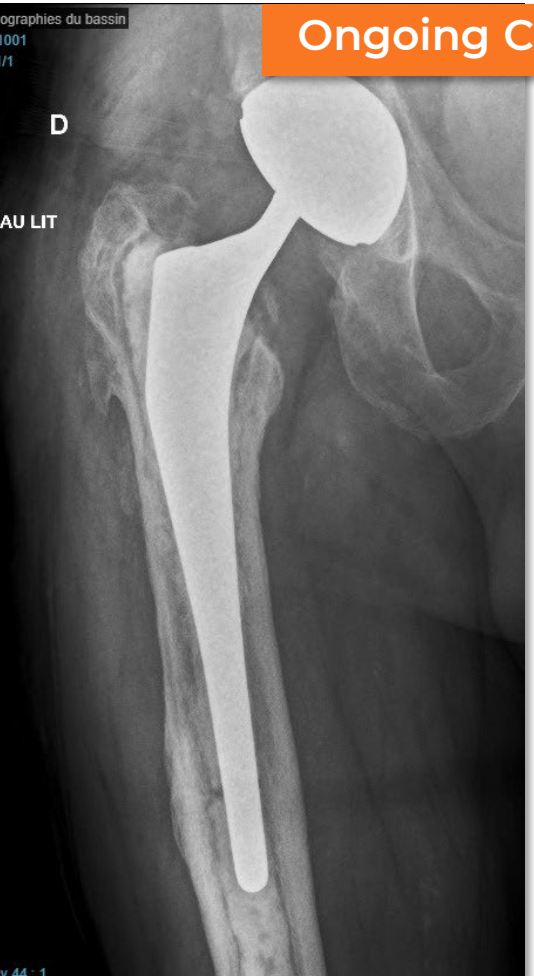


Ongoing Compassionate Use, Hôpital de la Croix Rousse, Lyon, France

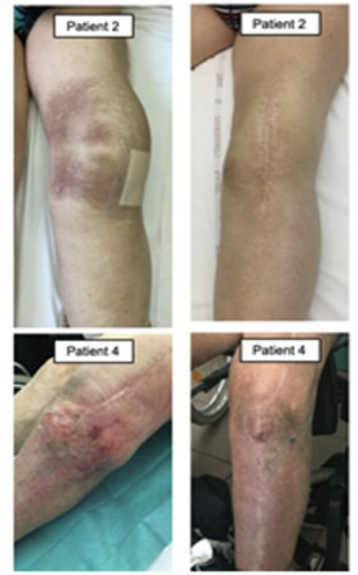
Ten patients treated with exebacase (intra-articular administration), as of YE

Long-term data from initial four patients with chronic knee infections included in ECCMID 2020 Abstract Book

- Two patients had clinical signs of septic arthritis (pictured); the two others had fistula. No adverse events occurred during arthroscopy
- Favorable clinical outcomes observed in the patients with septic arthritis, demonstrating disappearance of clinical signs for up to two years

Six additional patients treated in 2020

- Favorable clinical outcomes observed in the first two patients with chronic infection of hip prostheses at 3-month follow-up
- Favorable clinical outcomes observed in three patients treated without prior explantation at 3-month follow-up (one patient) and 6-month follow-up (two patients)



CF-370

Combating Gram-negative Pathogens, Including MDR and XDR Strains

CF-370 is Advancing to Next IND

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Based on proprietary lysin platform

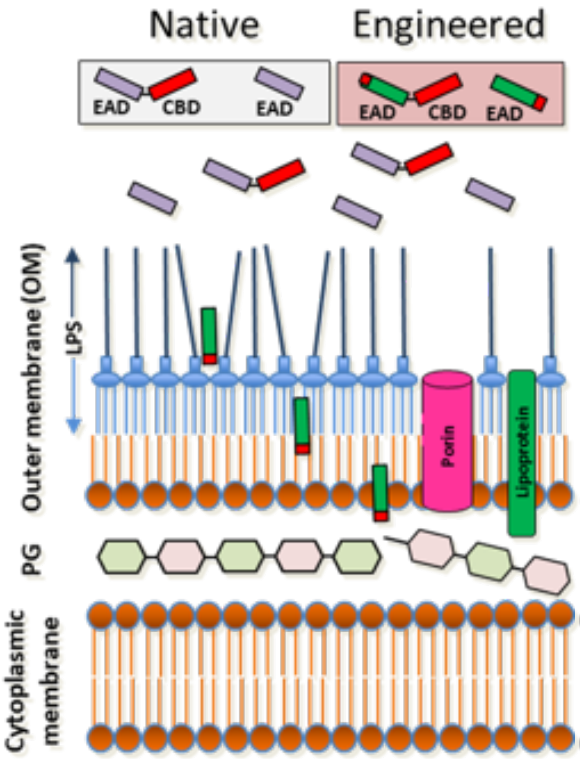
- First lysin engineered to bypass the outer membrane of GN bacteria and show potent activity in human blood

CF-370 currently in IND-enabling activities

- *In vitro* data demonstrates hallmark features of the lysin class
  - Rapid, potent and targeted bactericidal activity
  - Eradicated biofilms
  - Synergy observed with SOC antibiotics
  - Low propensity for resistance development
- *In vivo* activity observed in animal studies

Patent applications filed for GN lysin candidates

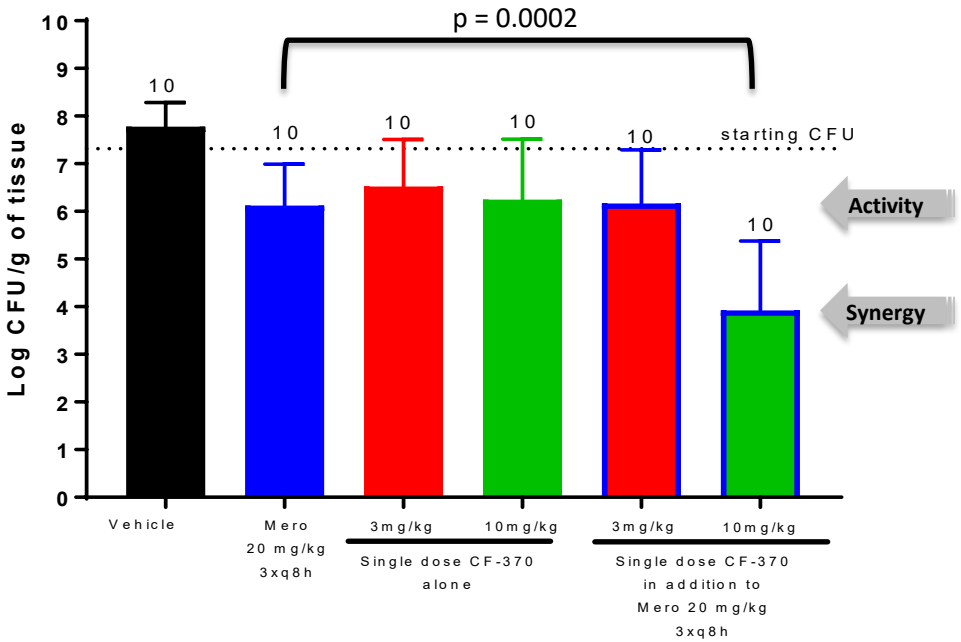
- U.S. Patent No. 10,988,520 issued for composition of matter and methods of treating Gram-negative bacterial infections



CF-370: Potent *In Vivo* Activity in *P. aeruginosa* Lung Infection Model

Single dose in rabbit lung infection model

Bacterial burden in lungs



- 100% of animals treated with CF-370 at 3 and 10 mg/kg alone or in addition to meropenem survived vs 40% in the vehicle control
- CF-370 alone demonstrated reduction in bacterial densities in the lung (p=0.0002 vs vehicle and similar to meropenem)
- CF-370 (10 mg/kg) synergized with meropenem to kill bacteria and further decrease bacterial density (p=0.0002 vs meropenem alone)

Source: Lehoux et al., ECCMID 2020 Abstract Book Publication, Abstract No. 1679

CF-370: Potent *In Vivo* Activity in *P. aeruginosa* Lung Infection Model

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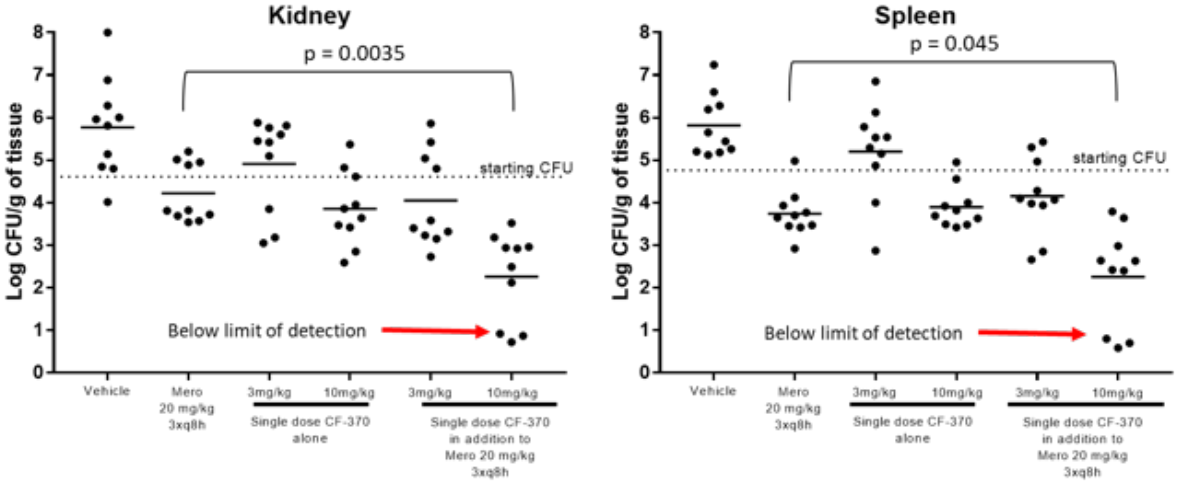
Single dose in rabbit lung infection model

Bacterial burden in secondary organs



- CF-370 significantly decreased bacterial densities in secondary organs
- Synergy with meropenem observed at 10 mg/kg
- 30% of the rats (CF-370 at 10 mg/kg + mero) had no bacteria detected in kidney and spleen (below LOD)

Source: Lehoux et al., ECCMID 2020 Abstract Book Publication, Abstract No. 1679

CF-370: Potent *In Vivo* Activity in *P. aeruginosa* Endocarditis Model

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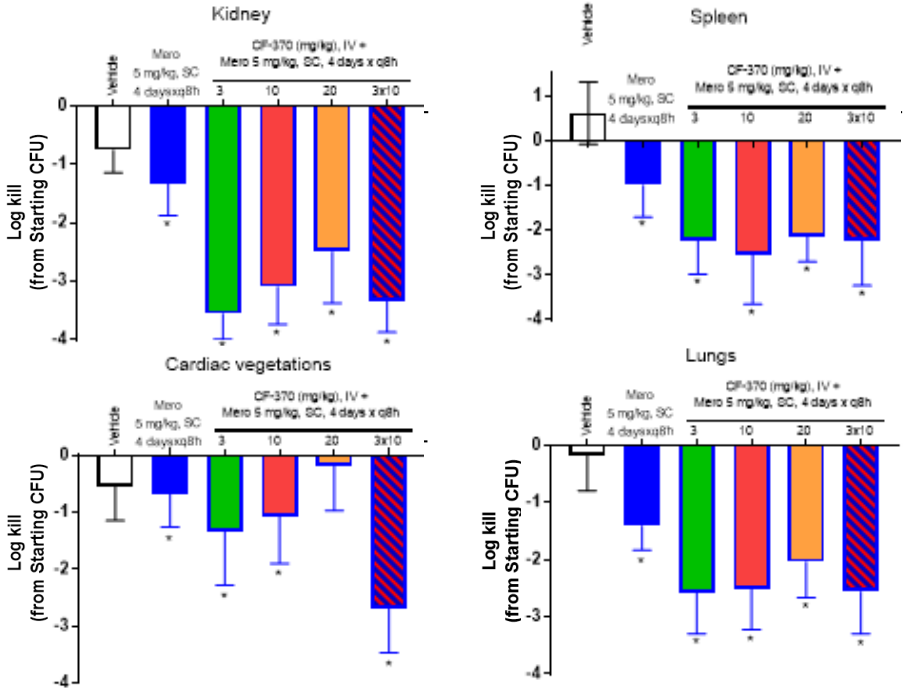
Single and multiple doses in rabbit infective endocarditis model

Log Kill (Log10 CFU reduction vs untreated) in all target organs



- Synergy was observed in all target organs (up to ≥ 2-Log kill)
- For kidney, spleen and lungs, CF-370 at all doses (+ Mero 5) provided more killing than mero alone (up to >2 log added kill)
- For the cardiac vegetations, with dense biofilm, the 3 days of CF-370 at 10 mg/kg (+ Mero 5) provided the most killing compared to mero alone (>2 log improvement; p=0.0007)

CF-370: Potent *In Vitro* Activity Against Gram- Pathogens

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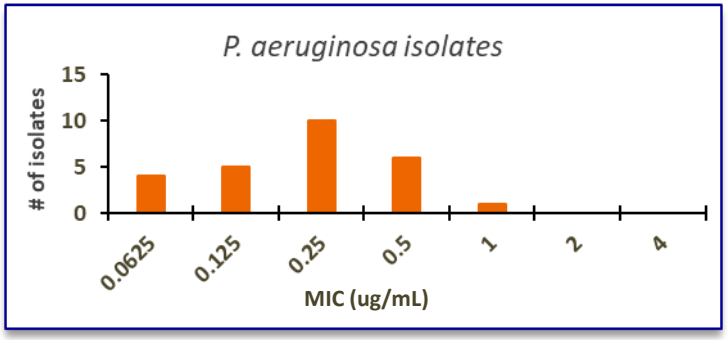
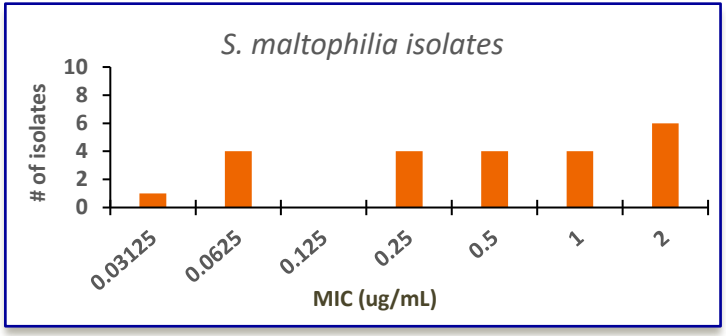
Minimal inhibitory concentrations (MICs) against CDC Antibiotic Resistance Bank

		MIC (µg/mL)											
Organism	n	0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	MIC_{50}	MIC_{90}	Range
P. aeruginosa	124					3	20	67	34			1	2	0.25 - 2
A. baumannii	80					6	27	44	3			1	1	0.25 - 2
E. coli	44		1	2	4	16	16	5				0.25	1	0.032 - 1
K. pneumoniae	73				3	7	10	16	27	10		2	4	0.125 - 4
E. cloacae	37	1				4	7	8	12	4	1	1	4	0.016 - 8

MICs against clinical isolates from Cystic Fibrosis patients





Source: Watson et al., World Microbe, June 2021 and internal data

Amurin Peptides

Potential Broad Spectrum Coverage of Gram-negative Pathogens

Amurins are Broadly Active Against GN Pathogens

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Novel lytic agents

- Potent activity observed in human blood
- Potential to improve clinical response and cure rates for resistant Gram-negative infections

Preclinical-stage program

- *In vitro* data demonstrates hallmark features of the lysin class
  - Rapid, potent and targeted bactericidal activity
  - Eradicated biofilms
  - Synergy observed with SOC antibiotics
- *In vivo* activity observed in animal studies

Patent applications filed

5 min *(P. aeruginosa)*

Broadly active

		MIC100 (ug/mL)				
Organism	**N**	**AM1**	**AM2**	**AM3**	**AM4**	**AM5**
P. aeruginosa	14	2	2	1	2	0.5
E. coli	10	2	1	2	1	0.5
E. cloacae	10	4	2	2	2	1
K. pneumoniae	10	2	2	1	2	1
A. baumannii	10	1	4	2	2	0.5
S. typhimurium	2	2	2	2	4	n.d.
S. aureus	10	>64	>64	>64	>64	>64

EM Analysis Demonstrates Mechanism of Action

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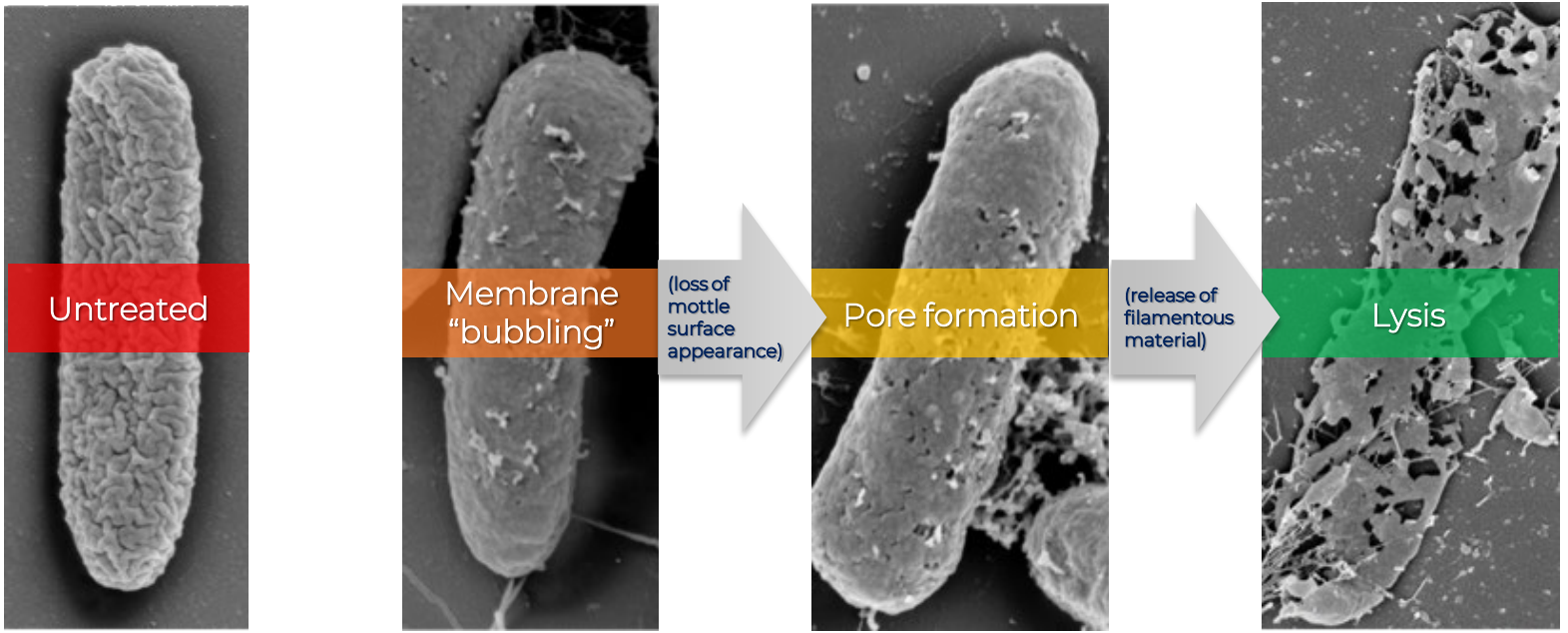
Three Step Process

20 minute treatment

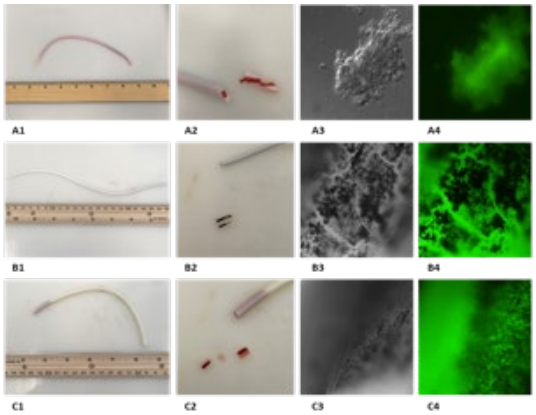


Amurin AM1 Eradicated *Stenotrophomonas maltophilia* Biofilms

ContraFect

- Performed in collaboration with Dr. Jamie Dwyer, Dept. of Nephrology (Vanderbilt)
- Hemodialysis catheters from patients with suspected CRBSI are shipped to ContraFect and immediately processed for treatment with AM1 *ex vivo*

- ❑ Explanted hemodialysis catheters (**Panels A1, B1, C1**)
- ❑ Exposure of intraluminal material (**Panels A2, B2, C2**)
- ❑ Analysis of intraluminal surface by differential interference contrast (DIC) microscopy, 2000x magnification (**Panels A3, B3, C3**)
- ❑ Same field as DIC, with visualization Biofilm Stain (**Panels A4, B4, C4**)



- Adherent mucoid biofilm observed within the lumen of all three catheters
- Bacterial clusters in biofilm-like structures (stained with calcein green) were observed adhering to internal lumen

- ❑ Equivalent segments were allotted into treatment groups and incubated at 37°C for 4 hours before homogenization and quantitative plating

Study groups	Log_{10} CFU/g of catheter		
	Catheter A	Catheter B	Catheter C
Treatment control	3.37	4.24	4.22
AM1 (1 µg/mL)	n.d.	<0.7	<0.7
AM1 (10 µg/mL)	<0.7	n.d.	n.d.
Meropenem (1 µg/mL)	n.d.	n.d.	3.16

Surviving bacteria were enumerated after 24 hrs of incubation at 37 °C. The limit of detection is 0.7 Log_{10} CFU/g of catheter

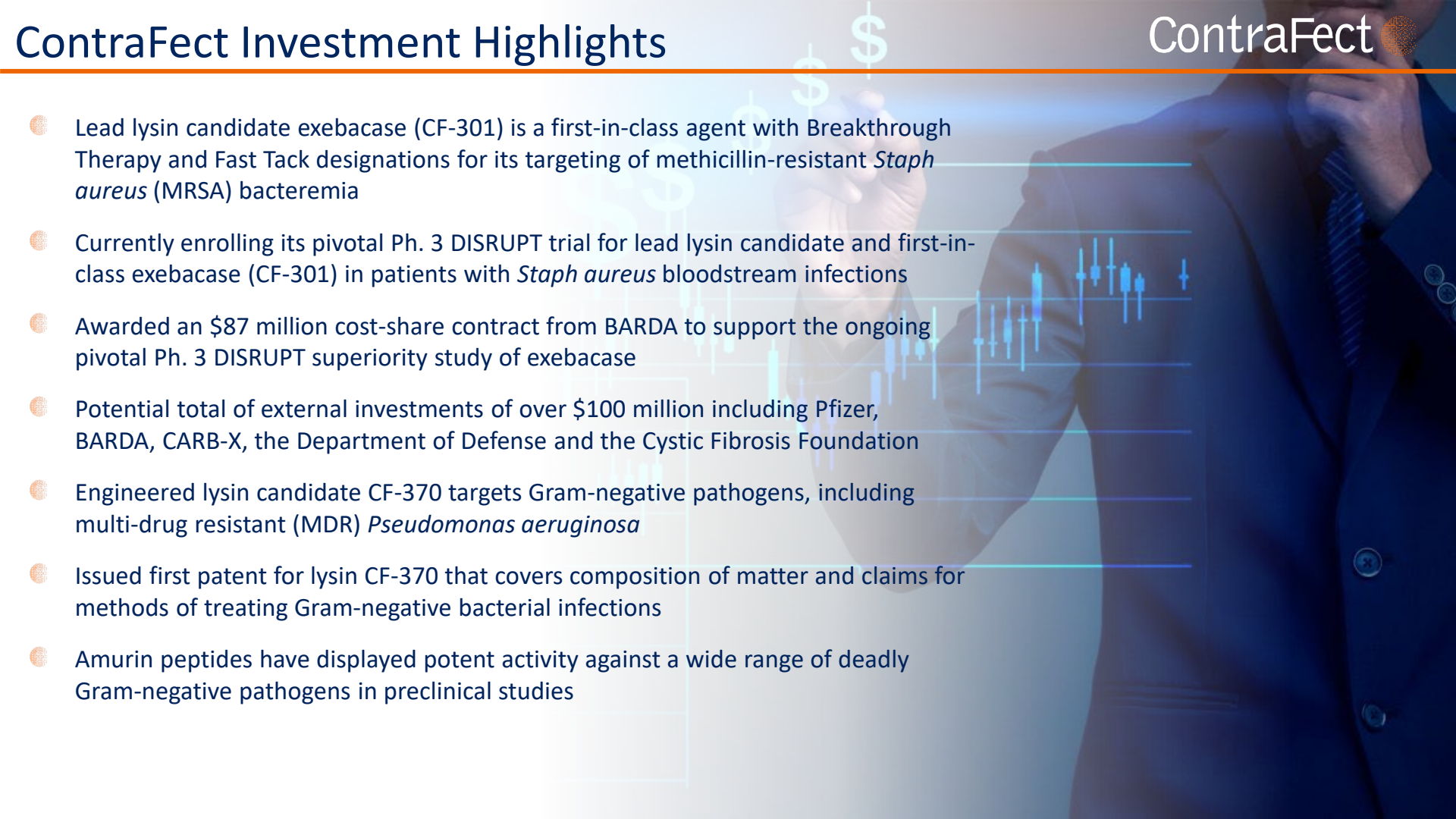
- ❑ Uniform colony morphology observed for isolates from each catheter
- ❑ Multiple isolates from each catheter were recovered and analyzed by 16S amplicon sequencing and MALDI-TOF to discern genus/species
- ❑ MICs were determined for each isolate set

		MIC (µg/mL)[a]	
Catheter	Organism	AM1	Meropenem
A	*S. maltophilia*	2	>32
B	*S. maltophilia*	1	>32
C	*S. maltophilia*	1	>32

Source: Oh et al., ASM-ESCMID 2019 Poster (#51)

Corporate Information

ContraFect Investment Highlights



- Lead lysin candidate exebacase (CF-301) is a first-in-class agent with Breakthrough Therapy and Fast Tack designations for its targeting of methicillin-resistant *Staph aureus* (MRSA) bacteremia
- Currently enrolling its pivotal Ph. 3 DISRUPT trial for lead lysin candidate and first-in-class exebacase (CF-301) in patients with *Staph aureus* bloodstream infections
- Awarded an $87 million cost-share contract from BARDA to support the ongoing pivotal Ph. 3 DISRUPT superiority study of exebacase
- Potential total of external investments of over $100 million including Pfizer, BARDA, CARB-X, the Department of Defense and the Cystic Fibrosis Foundation
- Engineered lysin candidate CF-370 targets Gram-negative pathogens, including multi-drug resistant (MDR) *Pseudomonas aeruginosa*
- Issued first patent for lysin CF-370 that covers composition of matter and claims for methods of treating Gram-negative bacterial infections
- Amurin peptides have displayed potent activity against a wide range of deadly Gram-negative pathogens in preclinical studies

Anticipated 2022 Milestones

ContraFect

Exebacase

- Complete interim futility analysis in the Phase 3 DISRUPT superiority study
- Initiate Phase 1b/2 study in patients with Staphylococcal prosthetic joint infections
- Complete enrollment for the Phase 3 DISRUPT study

CF-370

- Initiate Phase 1 studies, for development in HAP/VAP or Cystic Fibrosis patients

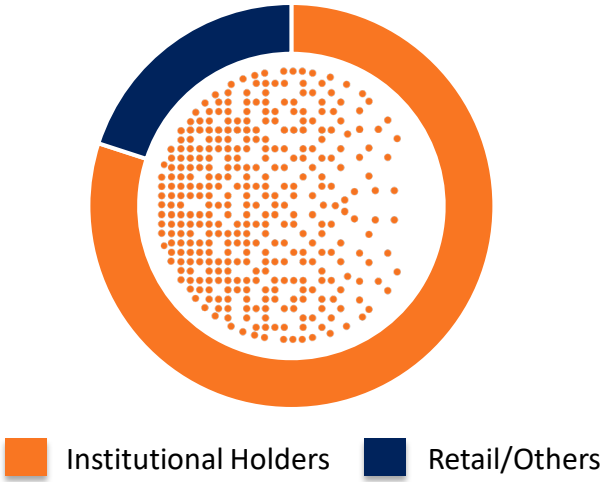
Amurin peptides

- Select IND candidate for broad spectrum Gram-negative coverage

Financial Information

Key Metrics		March 31, 2022
Cash and securities		$42.3 million
Total debt		——
Basic shares outstanding		39.3 million

Analyst Coverage	
Cantor	Louise Chen
Maxim	Jason McCarthy
Mizuho	Vamil Divan
SVB Securities	Roanna Ruiz



ContraFect

MOLECULAR TREATMENTS
FOR INFECTIOUS DISEASE

Differentiated, first-in-class direct lytic agents (DLAs) for life-threatening, drug-resistant infections

NASDAQ: CFRX