Exebacase (Lysin CF-301) Improved Clinical Responder Rates In Methicillin Resistant *Staphylococcus Aureus* (MRSA) Bacteremia Including Endocarditis Compared To Standard Of Care Antibiotics (SOC) Alone In A First-in-Patient Phase 2 study

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for the Exebacase Phase 2 Study Group
# Disclosures

<table>
<thead>
<tr>
<th>Nature of Relevant Financial Relationship</th>
<th>Commercial Interest</th>
</tr>
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<tbody>
<tr>
<td>Grant or research support</td>
<td>ContraFect; Cerexa/Actavis, Cubist/Merck; Genentech; Karius; MedImmune, NIH</td>
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<tr>
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<td>None</td>
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<td>Honoraria</td>
<td>Theravance; Green Cross</td>
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<tr>
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<td>Chair- Merck V710 Advisory Board Committee</td>
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<tr>
<td>Ownership Interest (e.g., stocks, stock options or other interests</td>
<td>NONE</td>
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<td>Other relevant financial interests</td>
<td>Patent pending in sepsis diagnostic</td>
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BACKGROUND

*S. aureus* Bacteremia (SAB) & Endocarditis

- Common & potentially lethal
- Standard of Care (SOC) therapy suboptimal
- MRSA particularly problematic
- New treatments are required
Lysins – A New Class of Antibacterials

Potent cell wall hydrolase enzymes derived from bacteriophage

- *In nature* – highly potent bacterial killer in bacteriophage armamentarium
- *New technology* – recombinantly produced and purified biologic therapy

Novel MOA – peptidoglycan hydrolysis leading to osmotic lysis

Hallmark Features

- Rapid, targeted, species-specific killing
- Potent eradication of biofilms
- Synergy with conventional antibiotics
- Low propensity for resistance
Study Design

- Phase II Randomized, double-blind, placebo-controlled, superiority design Proof of Concept study
  - Compares exebacase (EXE) + standard of care antibiotics (SOC) vs SOC

- Study population
  - Adults with documented S. aureus bacteremia including endocarditis

- Study objectives
  - Describe safety/tolerability
  - Estimate clinical outcome at Day 14 after study drug administration
  - Describe the pharmacokinetic parameters of EXE

- Primary endpoint – Clinical Responder Rate at Day 14
  - "Improvement/resolution of signs/symptoms, no new metastatic foci or complications, and no changes in antibiotic treatment or further medical intervention due to lack of response in patients alive at time of evaluation"
  - Determined by independent, blinded Adjudication Committee
Number of days of SOC antibiotic treatment varied widely: mean days, (range)

- EXE + SOC: 33.3 days, (2 - 181)
- SOC Alone: 30.5 days, (3 - 91)
Results
Patient Disposition

Randomized (3:2) 121

Exebacase + SOC

ITT 73

Safety 72

mITT 71

SOC Alone

ITT 48

Safety 47

mITT 45
Demographics were Similar in Both Groups

<table>
<thead>
<tr>
<th></th>
<th>Exebacase + SOC</th>
<th>SOC Alone</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N = 73</td>
<td>N = 48</td>
</tr>
<tr>
<td>Age (years, mean)</td>
<td>56.6</td>
<td>55.0</td>
</tr>
<tr>
<td>Age &gt; 50 (n, %)</td>
<td>47 (64.4)</td>
<td>34 (70.8)</td>
</tr>
<tr>
<td>Gender (n, %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>23 (31.5)</td>
<td>16 (33.3)</td>
</tr>
<tr>
<td>Male</td>
<td>50 (68.5)</td>
<td>32 (66.7)</td>
</tr>
<tr>
<td>Race (n, %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>14 (19.2)</td>
<td>8 (16.7)</td>
</tr>
<tr>
<td>White</td>
<td>51 (69.9)</td>
<td>30 (62.5)</td>
</tr>
<tr>
<td>Other</td>
<td>8 (11.0)</td>
<td>10 (20.8)</td>
</tr>
<tr>
<td>CrCl (ml/min, n, %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>28 (38.4)</td>
<td>12 (25.0)</td>
</tr>
<tr>
<td>30 to &lt;60</td>
<td>13 (17.8)</td>
<td>7 (14.6)</td>
</tr>
<tr>
<td>60 to &lt;90</td>
<td>5 (6.9)</td>
<td>4 (8.3)</td>
</tr>
<tr>
<td>≥90</td>
<td>24 (32.9)</td>
<td>23 (47.9)</td>
</tr>
<tr>
<td>Missing</td>
<td>3 (4.1)</td>
<td>2 (4.2)</td>
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## Risk Factors and Infecting Pathogen (mITT)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Exebacase + SOC N = 71</th>
<th>SOC Alone N = 45</th>
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<tbody>
<tr>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
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<tr>
<td>Poorly controlled diabetes mellitus(^1)</td>
<td>20 (32.3)</td>
<td>8 (20.5)</td>
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<tr>
<td>Injection drug use(^1)</td>
<td>6 (9.7)</td>
<td>5 (12.8)</td>
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<tr>
<td>Pre-existing valvular heart disease</td>
<td>1 (1.4)</td>
<td>3 (6.7)</td>
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<tr>
<td>Surgery within prior 30 days</td>
<td>11 (15.5)</td>
<td>5 (11.1)</td>
</tr>
<tr>
<td>Extravascular foreign material</td>
<td>9 (12.7)</td>
<td>9 (20.0)</td>
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<tr>
<td>Diagnosis of AIDS(^1)</td>
<td>2 (3.2)</td>
<td>1 (2.6)</td>
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<tr>
<td>Hemodialysis</td>
<td>21 (29.6)</td>
<td>8 (17.8)</td>
</tr>
<tr>
<td>SIRS(^1)</td>
<td>45 (72.6)</td>
<td>27 (69.2)</td>
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<tr>
<td><strong>Infecting Pathogen(^2)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA</td>
<td>27 (38.0)</td>
<td>16 (35.6)</td>
</tr>
<tr>
<td>MSSA</td>
<td>44 (62.0)</td>
<td>30 (66.7)</td>
</tr>
</tbody>
</table>

\(^1\) Risk factor not included in Protocol Amendment 4; denominator is 62 for exebacase and 39 for antibiotics alone.

\(^2\) One patient in the placebo group had both MRSA and MSSA.
Distribution of Final Diagnoses* Differed Between Groups

Overall (N = 116)
- uBAC = 16 (13.8%)
- cBAC = 78 (67.2%)
- RIE = 8 (6.9%)
- LIE = 14 (12.1%)

* As assessed by blinded Adjudication Committee

uBAC = uncomplicated bacteremia
cBAC = complicated bacteremia
RIE = right-sided endocarditis
LIE = left-sided endocarditis
Primary Efficacy Endpoint:
Clinical Responder Rates at Day 14 (mITT)

- Exebacase + SOC: 70.4% Responders, 29.6% Non-responders
- SOC antibiotics: 60.0% Responders, 40% Non-responders

p = 0.314

° indeterminates included with non-responders (3 in Exebacase group, 5 in antibiotics alone group)
Clinical Responder Rates at Day 14
Prespecified MRSA Subgroup Analysis

Exebacase + SOC
SOC Alone

MRSA

Exebacase + SOC: 20/27 (74.1%)
SOC Alone: 5/16 (31.3%)
p = 0.010

MSSA

Exebacase + SOC: 30/44 (68.2%)
SOC Alone: 22/30 (73.3%)

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Clinical Responder Rates at Day 14
Prespecified Final Diagnosis* Subgroups

* As assessed by blinded Adjudication Committee

- **cBAC**: 78.6% (33/42) Exebacase + SOC, 58.3% (21/36) SOC Alone
- **uBAC**: 92.3% (12/13) Exebacase + SOC, 33% (3/3) SOC Alone
- **LIE**: 66.7% (2/3) Exebacase + SOC, 18.2% (2/11) SOC Alone
- **RIE**: 60% (3/5) Exebacase + SOC, 33.3% (1/3) SOC Alone
Clinical Responder Rates at Day 7, EOT and TOC

<table>
<thead>
<tr>
<th></th>
<th>mITT</th>
<th>MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary Endpoint</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 7</td>
<td>68.9%</td>
<td>18.2%</td>
</tr>
<tr>
<td>EOT</td>
<td>62%</td>
<td>7.9%</td>
</tr>
<tr>
<td>TOC</td>
<td>55.6%</td>
<td>15.6%</td>
</tr>
<tr>
<td>Exploratory Endpoint</td>
<td></td>
<td></td>
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<tr>
<td>Day 7</td>
<td>43.8%</td>
<td>14.8%</td>
</tr>
<tr>
<td>EOT</td>
<td>43.8%</td>
<td>7.0%</td>
</tr>
<tr>
<td>TOC</td>
<td>48.2%</td>
<td>5.0%</td>
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## Safety Summary

<table>
<thead>
<tr>
<th>Event</th>
<th>Exebacase + SOC N = 72</th>
<th>SOC Alone N = 47</th>
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<tbody>
<tr>
<td><strong>TEAE through TOC</strong></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>TEAE through TOC</td>
<td>64 (88.9)</td>
<td>40 (85.1)</td>
</tr>
<tr>
<td>TEAE through Day 7</td>
<td>48 (66.7)</td>
<td>31 (66.0)</td>
</tr>
<tr>
<td>Serious TEAE through TOC</td>
<td>33 (45.8)</td>
<td>21 (44.7)</td>
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<tr>
<td>AE leading to discontinuation of study drug</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Total Deaths through TOC</td>
<td>14 (19.4)</td>
<td>7 (14.9)</td>
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TEAE = treatment emergent adverse event
Summary and Conclusions: Exebacase

- A first in class direct lytic agent

- In this Phase 2 trial, a single IV dose of exebacase + SOC to treat *S. aureus* SAB/IE:
  - was well tolerated
  - resulted in 42.8% higher clinical responder rate in prespecified MRSA subgroup vs SOC alone

- Results support further evaluation of exebacase in a definitive Phase 3 study
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Questions?