REVIVE-2:
A phase 3, Randomized, double-blind, multicenter study to evaluate the safety and efficacy of intravenous Iclaprim versus Vancomycin in the treatment of acute bacterial skin and skin structure infections suspected or confirmed to be due to Gram-positive pathogens

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on behalf of

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Disclosures

Consulting: The Medicines Company, Basilea Pharmaceutica, Theravance, Genentech

Scientific Advisory Board: Motif Bio

Adjudication committee: Achaogen, Basilea

Grant support: NIH, FDA

Royalties: UpToDate

Employment: Duke University
Iclaprim: A Promising Gram-positive Antibiotic

TARGETED MICROBIOLOGY
- Targeted Gram-positive spectrum including MRSA

TISSUE CONCENTRATION
- In sites of infection: skin and lung

STUDIED IN OVER 1,400 PATIENTS & HEALTHY VOLUNTEERS
- No nephrotoxicity in REVIVE trials
- No renal dosing
- No therapeutic drug monitoring

OPTIMIZED FIXED DOSING**
- Pharmacodynamic parameters associated with efficacy & safety

EVIDENCE OF CLINICAL EFFICACY***
- ABSSSI – non-inferior to vancomycin in 2 Phase 3 trials
- HABP/VABP

UNDERUTILIZED MOA
- Dihydrofolate reductase inhibitor designed to overcome TMP resistance

MRSA – methicillin-resistant Staphylococcus aureus; ABSSSI – acute bacterial skin & skin structure infections; HABP – hospital acquired bacterial pneumonia; VABP – ventilator associated bacterial pneumonia; * in vitro; ** 40mg for patients with moderate hepatic impairment; https://www.ncbi.nlm.nih.gov/pubmed/?term=huang+db+2017; ***Evidence of clinical efficacy based on clinical trials to date
REVIVE-2 Phase 3 Trial in ABSSSI: Clinical Response at ETP and TOC

**Intent-to-treat (ITT) population**

**Early Clinical Response (ECR)**
- Iclaprim: 78.3% (n=295)
- Vancomycin: 76.7% (n=305)

**Test of Cure (TOC)**
- Iclaprim: 77.6% (n=295)
- Vancomycin: 77.7% (n=305)

**Treatment difference**
- Iclaprim vs. Vancomycin:
  - ECR: +1.58% (95% CI: -5.10, 8.26)
  - TOC: -0.08% (95% CI: -6.74, 6.59)

* ECR: defined by FDA as ≥20% reduction in lesion size at 48-72h (Early Time Point) compared to baseline
## REVIVE-2 Phase 3 Trial in ABSSSI: Safety Results

<table>
<thead>
<tr>
<th></th>
<th>Iclaprim N=299</th>
<th>Vancomycin N=302</th>
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<tbody>
<tr>
<td>Study drug related TEAEs</td>
<td>42 (14.0%)</td>
<td>39 (12.9%)</td>
</tr>
<tr>
<td>TEAE related serious AEs</td>
<td>14 (4.7%)</td>
<td>12 (4.0%)</td>
</tr>
<tr>
<td>Mean QTcF prolongation msec (SD)</td>
<td>9.9 (14.6)</td>
<td>3.8 (16.3)</td>
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<tr>
<td>Mean serum creatinine change from baseline to TOC umol/L (SD)</td>
<td>0.7 (18.0)</td>
<td>7.7 (39.8)</td>
</tr>
<tr>
<td>Mean serum creatinine change from baseline to TOC, mg/dL (SD)</td>
<td>0.008 (0.20)</td>
<td>0.09 (0.45)</td>
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<tr>
<td>Deaths</td>
<td>0</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>TEAEs &gt;4%</td>
<td></td>
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</tr>
<tr>
<td>Nausea</td>
<td>17 (5.7%)</td>
<td>17 (5.6%)</td>
</tr>
<tr>
<td>Infusion site extravasation</td>
<td>13 (4.3%)</td>
<td>12 (4.0%)</td>
</tr>
<tr>
<td>Headache</td>
<td>7 (2.3%)</td>
<td>13 (4.3%)</td>
</tr>
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75% of adverse events in REVIVE-2 categorized as mild
REVIVE-2 Phase 3 Trial in ABSSSI: Conclusions

- Iclaprim was safe and efficacious in this Phase 3 trial for the treatment of ABSSSI.

- Iclaprim was well tolerated with a low rate of drug-related adverse events and met its primary endpoint of non-inferiority at ETP and also at TOC.

- Based on these results, iclaprim may be a valuable treatment for ABSSSI suspected or confirmed to be due to Gram-positive pathogens.