A Phase 1b/2a Randomized, Double-blind, Placebo-controlled, Multicenter Study Evaluating Nebulized Phage Therapy in Cystic Fibrosis Subjects with Chronic Pseudomonas aeruginosa Pulmonary Infection

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BACKGROUND
- Pseudomonas aeruginosa (PsA): most prevalent pulmonary pathogen in cystic fibrosis (CF) patients ≥ 35 years old; 50% of CF patients infected
- Most patients remain infected with PsA2, even after treatment with exelacafor / tezacaftor / ivacaftor
- Bacteriophage (phage) therapy: novel alternative or adjunct to antibiotics in chronic PsA infections

OBJECTIVES
- Phase 1b/2a clinical trial of nebulized phage cocktail (BX004-A) in CF subjects with chronic PsA pulmonary infection
  - Primary objective: safety & tolerability of BX004-A
  - Exploratory objectives: effect of BX004 on sputum PsA burden, PK of BX004-A in sputum, and clinical outcomes

METHODS
- Randomized, double-blind, placebo-controlled, multicenter study evaluating nebulized BX004-A in ≥ 32 outpatient adult CF subjects
- Clinically stable lung disease (FEV1 ≥ 40%) and chronic PsA pulmonary infections
- On inhaled antibiotics (tobramycin, aztreonam, or colistin)
- All Screening PsA morphotypes susceptible to ≥ 1 phage in BX004-A
- Part 1 (single-ascending and multiple dose portion): randomized (3:1) to BX004-A or placebo x 7 days, plus usual inhaled antibiotic
- Part 2 (multiple dose portion; n=24): randomized (2:1) to twice daily BX004-A or placebo x 10 days, plus usual inhaled antibiotic
- Safety follow-up until 6 months after last dose; independent Data Monitoring Committee oversees safety

RESULTS
- Phages: self-amplifying therapeutic agents

Part 1 (enrollment complete, n=9)

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>BX004-A (n=7)</th>
<th>Placebo (n=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean, years (range)</td>
<td>29.6 (20-37)</td>
<td>39.0 (25-53)</td>
</tr>
<tr>
<td>Male, %</td>
<td>57 (84.9)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>Female, %</td>
<td>28 (40.6)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>Israel, %</td>
<td>8/9 (89.9)</td>
<td>1/1 (11.1)</td>
</tr>
<tr>
<td>US, n (%)</td>
<td>1/9 (11.1)</td>
<td>2/2 (100)</td>
</tr>
<tr>
<td>BMI (kg/m²), mean (range)</td>
<td>22.8 (18.7-26.7)</td>
<td>24.6 (24.4-24.8)</td>
</tr>
<tr>
<td>CRTF modulators, n (%)</td>
<td>3/9 (33.3)</td>
<td>0/9 (0)</td>
</tr>
<tr>
<td>% predicted FEV1, mean (range)</td>
<td>66 (45-83)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>PsA log₁₀ Po2 CFU/g on Day 1; mean (range)</td>
<td>7.4 (4.2-8.5)</td>
<td>7.9 (7.8-8.0)</td>
</tr>
</tbody>
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Part 1: Topline results after D15 visit
- Study drug well-tolerated; no adverse events related to study drug
- No premature discontinuations from study drug or study
- No emerging resistance to BX004-A in treated subjects
- Phage detected in sputum of all BX004-A subjects during treatment, including in several subjects up to Day 15

RESULTS (Cont’d)

Part 1 Microbiologic Efficacy of BX004-A or placebo in addition to inhaled antibiotics. Mean PsA CFU reduction at Day 15 vs Baseline:
-1.42 log₁₀ (BX004-A) vs -0.28 log₁₀ (placebo)

Part 2 (ongoing enrollment)

<table>
<thead>
<tr>
<th>Visit</th>
<th>BX004-A (n=3)</th>
<th>Placebo (n=1)</th>
</tr>
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<tbody>
<tr>
<td>Day 1 baseline</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Day 8 End of Treatment</td>
<td>▲▲▲▲▲▲</td>
<td>ND</td>
</tr>
<tr>
<td>Day 15</td>
<td>▲▲</td>
<td>ND</td>
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</tbody>
</table>

No D: Not Detected

- Subjects with any BX004-A phage detected in sputum

CONCLUSION
- Phase 1b/2a clinical trial assessing safety, tolerability, and efficacy of BX004-A in CF subjects with chronic PsA pulmonary infection, showed that all subjects in Part 1 and Part 2 (to date) had high levels of Screening PsA, with all PsA morphotypes susceptible to BX004-A phage cocktail
- Part 1 topline: Study drug well-tolerated with notable microbiologic efficacy in BX004-A treated subjects
- Part 2 ongoing: Subjects enrolled to date have comparable demographics and baseline characteristics as Part 1

REFERENCES
1 Cystic Fibrosis Foundation Patient Registry, 2021 Annual Data Report, Bethesda, Maryland, ©2022 Cystic Fibrosis Foundation

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DISCLOSURES
URI, MKH, XU, EK., HN, IW, HSL, TG, JJ, NB, TA, OB, VL, YZ, YZ, MG, RV, MB are current or former employees of BiomX and own stock; EkE. is a consultant for BiomX