P095

# 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[1]
- **Most patients remain infected** with *PsA*[2] , even after treatment with elexacaftor / tezacaftor / ivacaftor
- Bacteriophage (**phage**) therapy: novel **alternative or adjunct to antibiotics** in chronic *PsA* infections

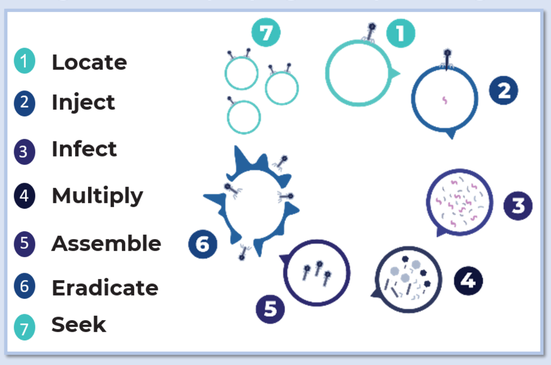
## OBJECTIVES

- **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-A 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

**Phages: self-amplifying therapeutic agents**




Nebulizer

## RESULTS

**Part 1** (enrollment complete, n=9)

| Baseline Characteristic | BX004-A (n=7) | Placebo (n=2) |
|---|---|---|
| Age, mean, years (range) | 29.6 (20-37) | 39.0 (25-53) |
| Male, n (%)<br>Female, n (%) | 5 (71.4)<br>2 (28.6) | 1 (50)<br>1 (50) |
| Israel, n (%)<br>US, n (%) | 8/9 (88.9)<br>1/9 (11.1) | |
| Race: white, n (%) | 7 (100) | 2 (100) |
| BMI (kg/m²), mean (range) | 22.8 (18.7-26.7) | 24.6 (24.4-24.8) |
| CFTR modulators, n (%) | 3/9 (33.3) | |
| % predicted FEV1; mean (range) | 66 (45-83) | |
| *P. aeruginosa** $log_{10}$ CFU/g on Day 1; mean (range) | 7.4 (4.2-8.5) | 7.9 (7.8-8.0) |

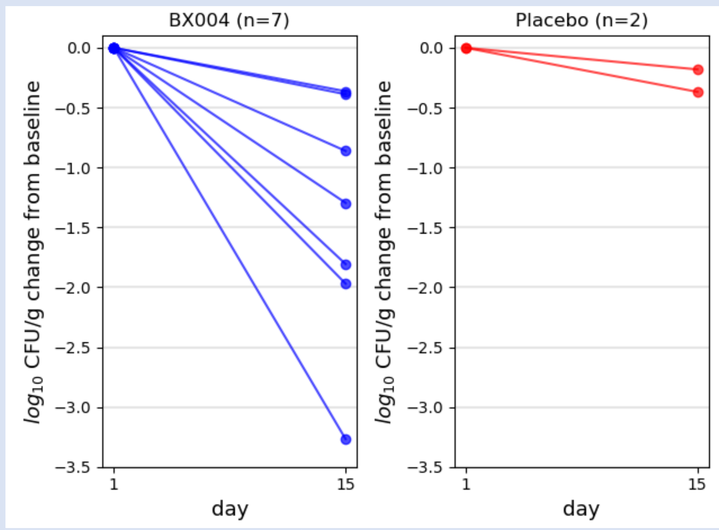
*Multidrug-resistant (MDR) *PsA* in sputum: n=1 (BX004-A); n=1 (placebo);
Extensively drug-resistant (XDR) *PsA* in sputum: n=1 (BX004-A); n=1 (placebo)

**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 $log_{10}$ (BX004-A) vs -0.28 $log_{10}$ (placebo)




| | BX004-A | Placebo |
|---|---|---|
| n | 7 | 2 |
| **Mean *PsA* CFU Reduction at D15 (range)** | **-1.42** $log_{10}$ (-3.27 to -0.37) | **-0.28** $log_{10}$ (-0.37 to -0.18) |

**Part 1 Pharmacokinetics**
Phages detected in all subjects treated with BX004-A

| Visit | BX004-A (n=7) | Placebo (n=2) |
|---|---|---|
| **Day 1** Baseline | ND | ND |
| **Day 8** End of Treatment | ▲▲▲▲▲▲ | ND |
| **Day 15** | ▲▲ | ND |

ND: Not Detected
▲: Subjects with any BX004-A phage detected in sputum

**Part 2** (*ongoing* enrollment)

| Baseline Characteristic | Interim Data |
|---|---|
| Age, mean, years (range) | 34.7 (19-52) |
| Male, %<br>Female, % | 53.8<br>46.2 |
| Israel, %<br>US, % | 38.5<br>61.5 |
| Race: white, % | 92.3 |
| BMI (kg/m²), mean (range) | 23.2 (19.3-27.1) |
| CFTR modulators, % | 69 |
| % predicted FEV1; mean (range) | 66 (45-107) |
| *P. aeruginosa* $log_{10}$ CFU/g on Screening; mean (range) | 7.3 (4.2-8.2) |

## 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
[2] Nichols DP, et al. *J Clin Invest.* 2023 Mar 28.

## ACKNOWLEDGEMENTS

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## DISCLOSURES

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

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BMI: body mass index; CFTR: CF transmembrane conductance regulator; FEV1: forced expiratory volume in 1 second; CFU/gram: colony-forming units/g; MDR *PsA*: non-susceptible to ≥ 1 agent in ≥ 3 antimicrobial categories; XDR *PsA*: non-susceptible to ≥ 1 agent in all but ≤ 2 antimicrobial categories