A Novel Treatment for Chronic *Pseudomonas aeruginosa* Pulmonary Infection in CF Subjects: A Phase 1b/2a Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate Phage Therapy

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Background

Pseudomonas aeruginosa

- Causes **chronic** and **difficult-to-treat infections** in cystic fibrosis (CF) patients
- Associated with **lower FEV1** at all ages [1]
- Increased hospitalizations
- Decreased quality of life

After **prolonged and repeated antibiotic** courses, increased **antibiotic resistance** → lower efficacy

Most patients remain infected with *P. aeruginosa* [2], even after treatment with elexacaftor / tezacaftor / ivacaftor

Bacteriophage (**phage**) therapy

- Targeted therapy: binds **only** to **specific bacterial** strains; does not bind to human cells

Novel **alternative or adjunct** to **antibiotics**

Phage have been successfully used in **compassionate use** for **pulmonary** infections, including in CF patients [3, 4]

BX004-A: BiomX proprietary **phage cocktail** targeting *P. aeruginosa*

Objectives

Primary objective: safety & tolerability of BX004-A

Exploratory objectives

- Effect of BX004-A on sputum *P. aeruginosa* burden
- Pharmacokinetics (PK) of BX004-A in sputum
- Clinical outcomes

Methods

- Multicenter study evaluating nebulized BX004-A in **outpatient adult CF subjects (sites in US, EU, Israel)**
- **Part 1 (n=9):** Randomized (3:1) to BX004-A or placebo x **7 days**, on top of standard of care
- **Part 2 (minimum n=24):** Randomized (2:1) to twice daily BX004-A or placebo **x 10 days**, on top of standard of care
- *P. aeruginosa* strains sequenced by **next-generation sequencing**

Results

Part 1: Topline Results

Baseline Characteristic (Part 1)	BX004-A (n=7)	Placebo (n=2)
Age, mean, years (range)	29.6 (20-37)	39.0 (25-53)
Male, n (%) Female, n (%)	5 (71.4) 2 (28.6)	1 (50) 1 (50)
Israel, n (%) US, n (%)	8/9 (88.9) 1/9 (11.1)	
Race: white, n (%)	7 (100)	2 (100)
BMI (kg/m^2), 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) *P. aeruginosa* in sputum: n=1 (BX004-A); n=1 (placebo); Extensively drug-resistant (XDR) *P. aeruginosa* in sputum: n=1 (BX004-A); n=1 (placebo)

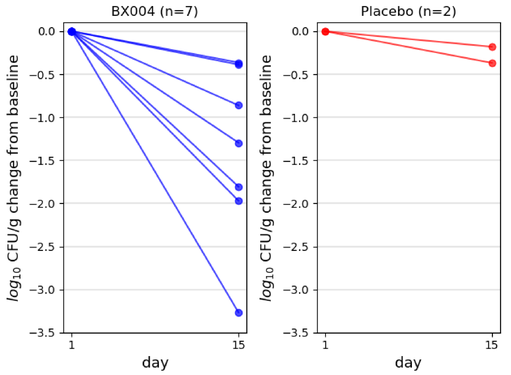
Results (cont'd)

Part 1: Safety

- Study drug was **well-tolerated**
  - No premature discontinuations from study drug or study
- **No adverse events related to study drug**
- **No adverse events of special interest** (acute pulmonary exacerbations or pulmonary worsening after study drug administration)

Part 1: Microbiologic Efficacy

- Mean *P. aeruginosa* CFU reduction at Day 15 vs Baseline: **-1.42 $\log_{10}$** (BX004-A) vs **-0.28 $\log_{10}$** (placebo)



	BX004-A (n=7)	Placebo (n=2)
Mean *P. aeruginosa* CFU Reduction at D15 (range)	**-1.42** $\log_{10}$ (-3.27 to -0.37)	**-0.28** $\log_{10}$ (-0.37 to -0.18)

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

Results (cont'd)

- **Bacterial genomic analysis**: each patient consistently colonized with **same genotypic strain of *P. aeruginosa***, from **Screening** up to **end of therapy**
- **No emerging resistance to BX004-A** during or after treatment

Part 1: Pharmacokinetics in **Sputum**

- **No phages** detected at **Baseline** (before study drug) in subjects treated with **BX004-A**
- **Phage detected in sputum of all** BX004-A subjects during **treatment** (at any timepoint), including in several subjects up to Day 15 (one week after last dose)
- **No phages** detected in **placebo-treated** subjects

Part 2 (*Ongoing*)

Baseline Characteristic (Part 2)	Interim Data
Age, mean, years (range)	34.3 (19-68)
Male, % Female, %	55 45
US, % Israel, % EU, %	50 25 25
Race: white, %	90
BMI (kg/m^2), mean (range)	22.7 (17.2-27.1)
CFTR modulators, %	60
% predicted FEV1; mean (range)	62 (45-107)
P. aeruginosa $\log_{10}$ CFU/g on Screening; mean (range)	6.3 (4.2-8.2)

Conclusions

Part 1 topline: Study drug well-tolerated; mean *P. aeruginosa* reduction at **Day 15** (vs Baseline): **-1.42 $\log_{10}$ CFU/g** (BX004) **vs -0.28 $\log_{10}$ CFU/g** (placebo) **on top of standard of care inhaled antibiotics**

Part 2 (*ongoing*): Subjects enrolled to date have **similar baseline characteristics** as Part 1, with more subjects from US & EU

Conflict of Interest Disclosure: UR is an employee of BiomX and owns stock

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References

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