WS06.06

5 – 8 JUNE 2024
GLASGOW, UNITED KINGDOM

47th EUROPEAN CYSTIC FIBROSIS CONFERENCE

Safety and efficacy of a nebulized phage cocktail in cystic fibrosis patients with chronic *Pseudomonas aeruginosa* pulmonary infection: a phase 1b/2a randomized, double-blind, placebo-controlled study

Eitan Kerem[1], Urania Rappo[2], Ariel Cohen[3], Iris Maimon[3], Edith Kario[3], Jenia Gold[3], Hadas-Tamar Nevenzal[3], Inbal Levy-Saar[3], Tal Cohen[3], Iddo N. Weiner[3], Hila Sberro Livnat[3], Ilya Vainberg Slutskin[3], Jagoda Jablonska[3], Ron Mordoch[3], Tim Axelrod[3], Ori Bahar [3], Nufar Buchshtab[3], Vered Lev[3], Yaron Tzur[3], Yulia Zarchin[3], Myriam Golembo[3], Regis Vilchez[2], Merav Bassan[3]

[1]Department of Pediatrics and CF Center, Hadassah University Hospital, Jerusalem, Israel; [2]BiomX Inc., Cambridge, Massachusetts, US; [3] BiomX Ltd, Ness Ziona, Israel

CONFLICT OF INTEREST(S):

- **E Kerem** is a consultant for BiomX
- Other co-authors are current or former employees of BiomX and may own company securities

BACKGROUND

- *Pseudomonas aeruginosa* (Pa): associated with pulmonary exacerbations in people with cystic fibrosis (PwCF) even in the era of elexacaftor/tezacaftor/ivacaftor (ETI)

- **Bacteriophage (phage) therapy:** novel **alternative or adjunct** to antibiotics

- **Phase 1b/2a clinical trial of nebulized phage cocktail (BX004-A)** in pwCF with **chronic Pa pulmonary infection**

    - **Primary objective**: safety & tolerability of BX004-A

    - **Exploratory objectives**: efficacy of BX004-A on sputum Pa burden and clinical outcomes

Nebulizer

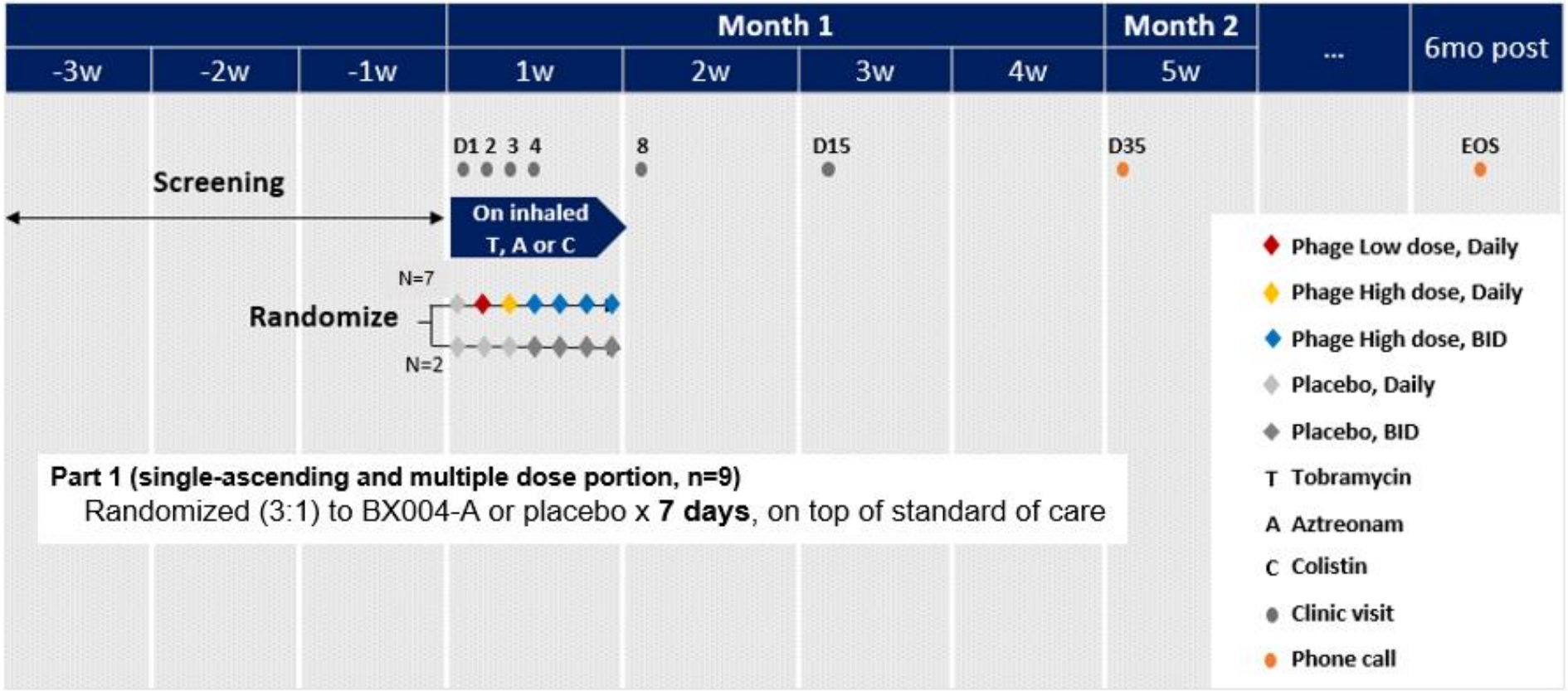
METHODS

Ph1b/2a Randomized Clinical Trial of Nebulized Phage for *Pseudomonas aeruginosa* Pulmonary Infection

- Outpatient adult CF subjects (total n=43)
- Key Inclusion Criteria
  - Clinically stable lung disease: **Forced Expiratory Volume in 1 sec (FEV1) ≥ 40% predicted**
  - **Chronic Pa pulmonary infection**: ≥ 1 sputum or throat culture in past 12 months positive for Pa (in addition to Screening sputum culture)
  - On **chronic inhaled** antibiotics (**tobramycin, aztreonam, or colistin**) as standard of care (SOC)
  - Screening **sputum Pa level ≥ 10^5** colony-forming unit (CFU/g)
  - All Screening Pa morphotypes **susceptible to ≥ 1 phage** in BX004-A
- **Part 1 (n=9):** randomized (3:1) to BX004-A or placebo **x7 days**, plus usual inhaled antibiotic
  - D1-3: single ascending doses (D1 placebo x1 → D2 low dose x1 → D3 high dose x1)
  - D4-7: twice daily high dose x 4 days
- **Part 2 (n=34):** randomized (2:1) to twice daily BX004-A or placebo **x10 days**, plus usual inhaled antibiotic
  - D1-10: twice daily high dose x 10 days

PART 1: **STUDY DESIGN**

Randomized (3:1) to single-ascending dose and multiple doses

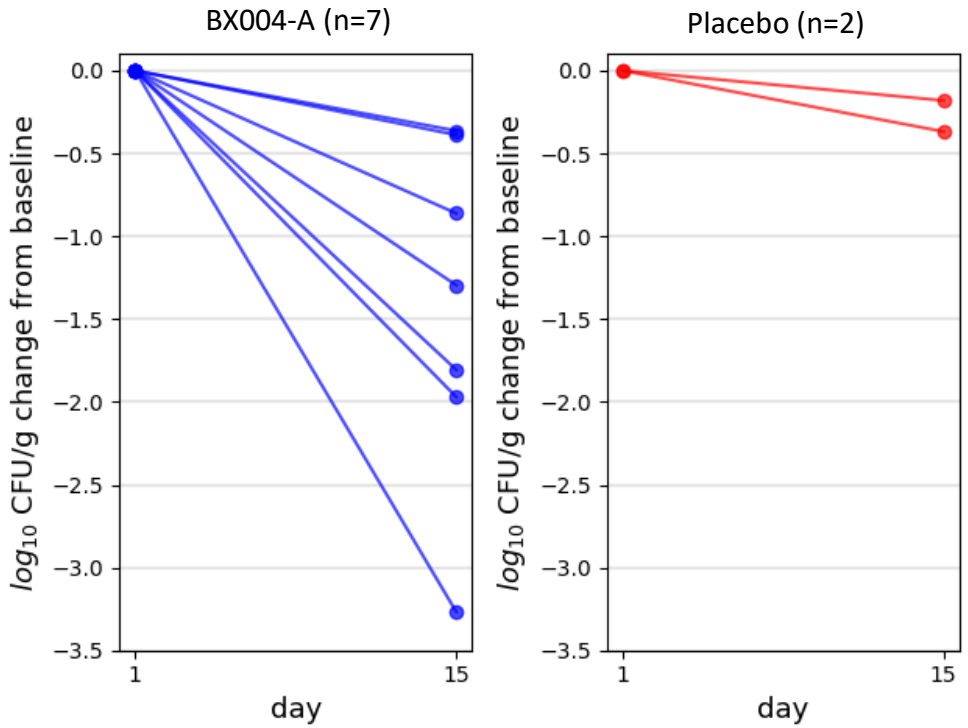


- n=7 nebulized BX004-A phage therapy
- n=2 nebulized placebo
- Treatment duration: 7 days (3 single ascending dosing days, 4 multiple dosing days)

PART 1: **RESULTS**

Part 1 (n=9)

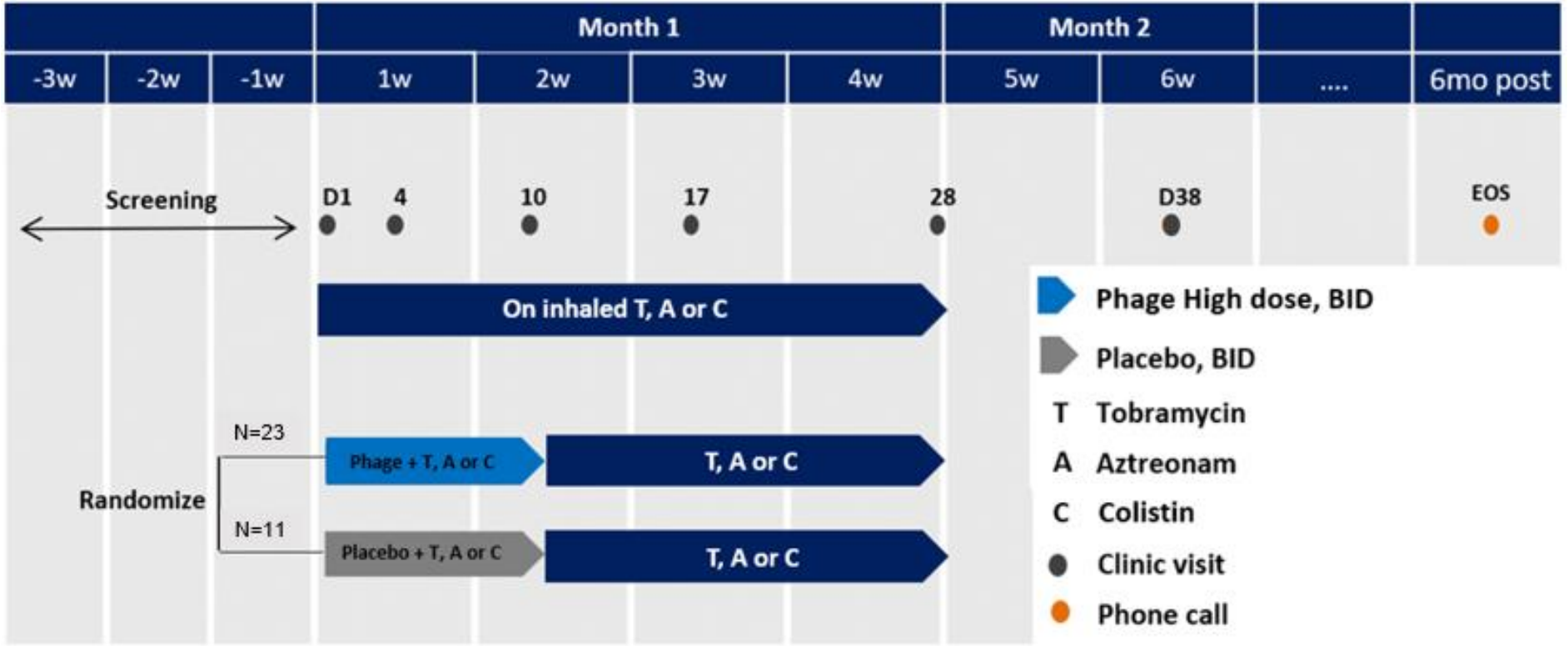
- Mean sputum Pa colony forming unit (CFU/g) change from baseline at D15 was **-1.42 log (BX004-A**, n=7) vs. **-0.28 log (placebo**, n=2)



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

PART 2: **STUDY DESIGN**

Randomized (2:1) to twice daily BX004-A or placebo x 10d, on top of standard of care



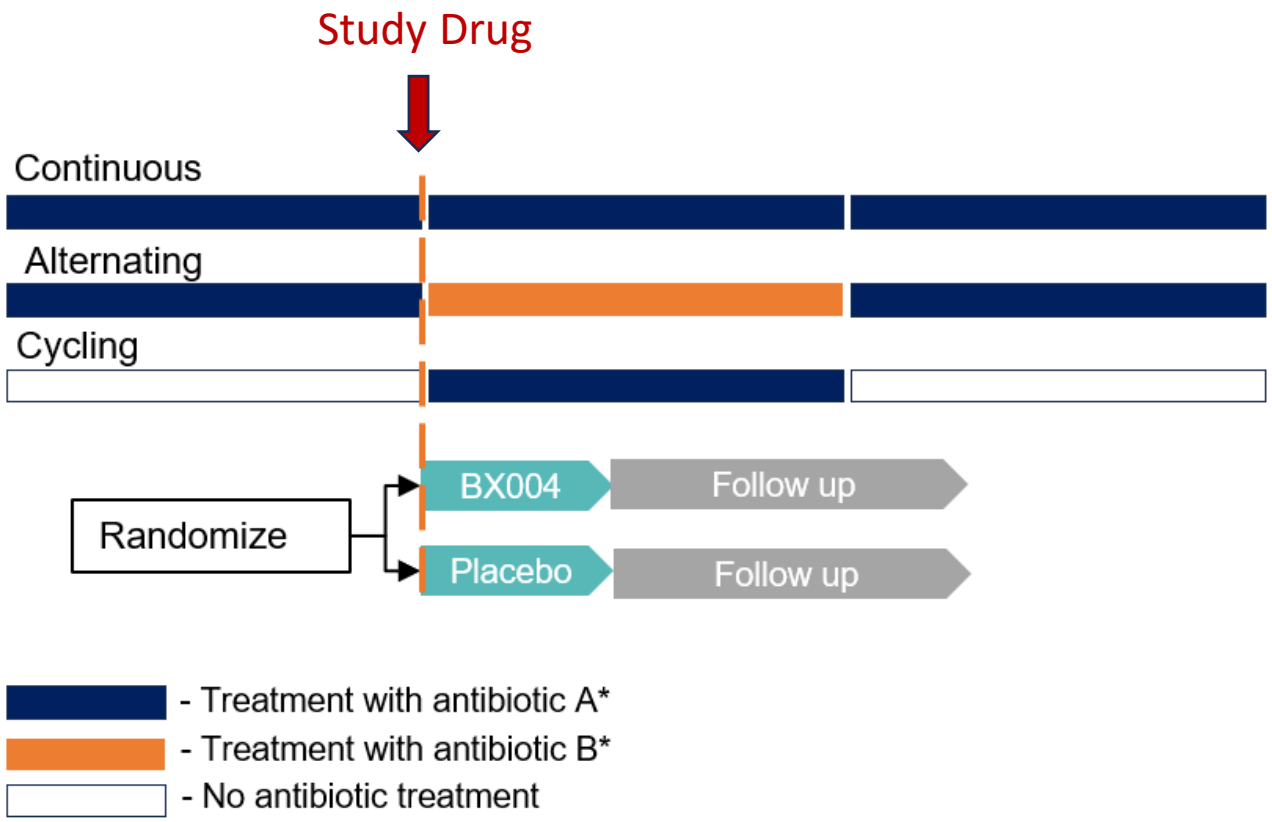
- **Larger sample size** than Part 1 (n=23 on BX004-A, n=11 on placebo)
- **Longer duration** of therapy (**10 days**), high dose twice daily
- **Later in-clinic follow-up** to at least Day 28 (18 days after last dose)

PART 2: **STUDY DESIGN**

Timing of study drug with SOC chronic inhaled antibiotics

Inhaled antibiotic regimens in CF

- **Continuous**: **same** inhaled antibiotic before, during, and after study drug
- **Alternating**: inhaled antibiotic A x 28 days, **alternating** with inhaled antibiotic B x 28 days
- **Cycling**: **off-cycle** with no inhaled antibiotic x 28 days then **on-cycle** x 28 days
- **Study drug** on Day 1 started with **on-cycle** (if on cycling antibiotic) or next **alternating antibiotic** (if on alternating regimen)



*Tobramycin or Aztreonam or Colistin

PART 2 (n=34): **KEY BASELINE CHARACTERISTICS** (Safety Population)

Characteristic	BX004-A (N=23)	Placebo (N=11)	P-value
Age, mean, years (SD)	36.8 (12.06)	33.1 (8.9)	0.37
Male, n (%)	14 (60.9)	5 (45.5)	0.49
EU (Spain, Netherlands, Czech Republic), n (%) US, n (%) Israel, n (%)	11 (47.9) 7 (30.4) 5 (21.7)	6 (54.5) 3 (27.3) 2 (18.2)	0.71 0.71 0.81
CFTR modulators, n (%)	17 (73.9)	9 (81.8)	0.94
Inhaled antibiotic (during study drug) Colistin, n (%) Tobramycin, n (%) Aztreonam, n (%)	 12 (52.2) 8 (34.8) 3 (13)	 5 (45.5) 4 (36.4) 2 (18.2)	 0.71 0.92 0.69
Type of inhaled antibiotic regimen Continuous, n (%) Cycling, n (%) Alternating, n (%)	 9 (39.1) 8 (34.8) 6 (26.1)	 6 (54.5) 3 (27.3) 2 (18.2)	 0.39 0.66 0.61
% Predicted FEV1: mean (SD), n	63.8 (21.07), 22	59.0 (17.48), 11	0.52
P. aeruginosa $\log_{10}$ CFU/g in sputum on D1; mean (SD), n* Range	6.65 (1.39), 21 3.38-8.13	6.8 (1.5), 10 3.34-8.04	0.35

*modified intent-to-treat population; SD: standard deviation; CFTR: CF transmembrane conductance regulator

PART 2: **RESULTS**

Part 2 (n=34)

- BX004-A, n=23; Placebo, n=11
- In subjects with quantitative sputum Pa CFU at baseline
  - **3/21 (14.3%) on BX004-A** had a **negative Pa sputum culture at D10** (end of treatment), with prior duration of chronic Pa 13-35 years, vs **0/10 (0%) on placebo**

Patient	Duration of Pa infection (years)	Baseline Pa in sputum (CFU/g)
1	**18**	**$2.40x10^3$**
2	**13**	**$5.60x10^7$**
3*	**35**	**$1.09x10^7$**

*Subject had negative sputum culture for *P. aeruginosa* at D4, D10, D28, D38, D63, D151 and at most recent standard of care clinic visit D167

PART 2: **RESULTS** (cont'd)

In subjects on **continuous** inhaled antibiotics (rather than cycling / alternating regimens)

- Mean **sputum Pa CFU reduction at D10**: **-2.91 log (BX004-A**, n=7) vs **-0.10 log (placebo,** n=5), Figure 1

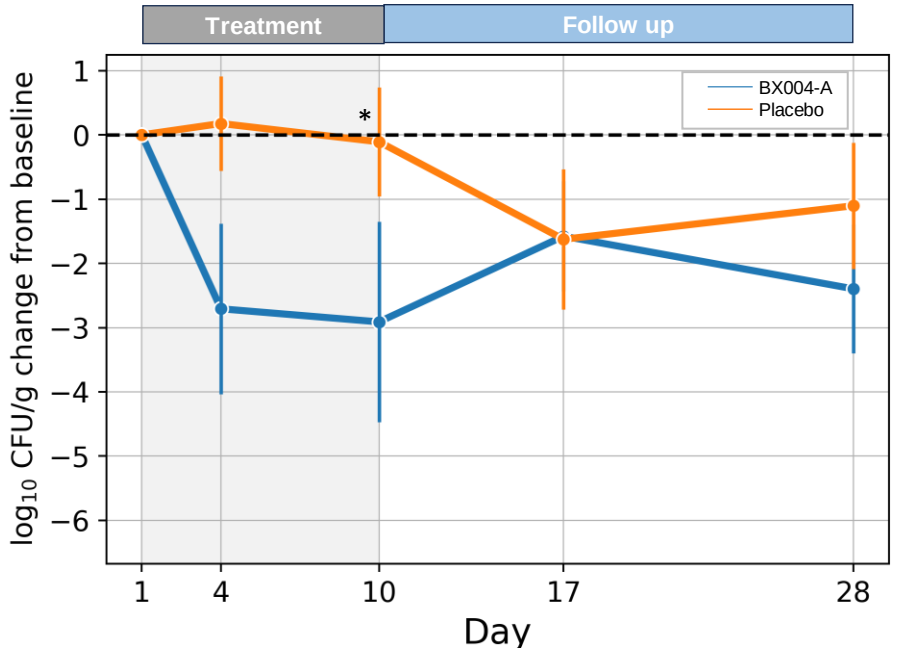


Figure 1: Mean (SE) **sputum Pa CFU/g** log change from baseline in subjects on **continuous** inhaled antibiotics

* p=0.16

PART 2: **RESULTS** (cont'd)

In subjects on **continuous** inhaled antibiotics and **on ETI**

- Mean **sputum Pa CFU reduction at D10 -4.82 log (BX004-A,** n=5) vs **-0.11 log (placebo,** n=5) ($p<0.05$), Figure 2

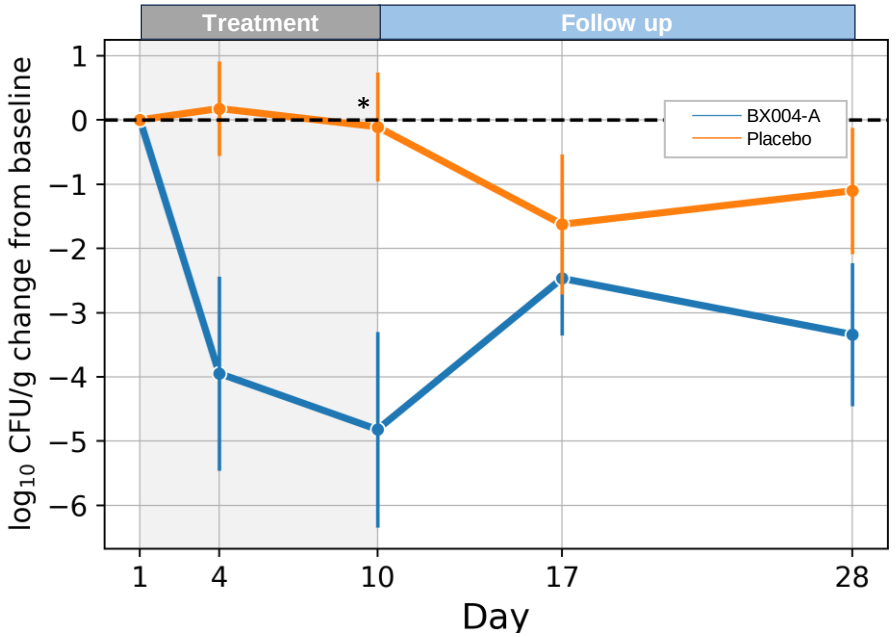


Figure 2: Mean (SE) **sputum Pa CFU/g** log change from baseline in subjects on **continuous** inhaled antibiotics and on **ETI**

* p=0.02

PART 2: **RESULTS** (cont'd)

In subjects on **continuous** inhaled antibiotics, **on ETI** and with **FEV_1 <70%**

- Mean **sputum Pa CFU reduction at D10: -3.84 log (BX004-A,** n=4) vs **-1.03 log (placebo**, n=3)**,** Figure 3
- Relative **FEV_1 improvement of +8.89%** at D17 between groups (change from baseline +5.66% in BX004-A vs -3.23% in placebo), Figure 4 (BX004-A, n=4; placebo, n =4)

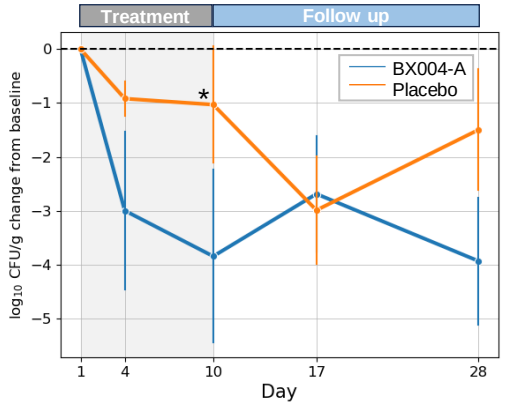


Figure 3: Mean (SE) **sputum Pa CFU/g** log change from baseline in subjects on **continuous** inhaled antibiotics, on **ETI** and with **FEV1 <70%**

* *p*=0.22

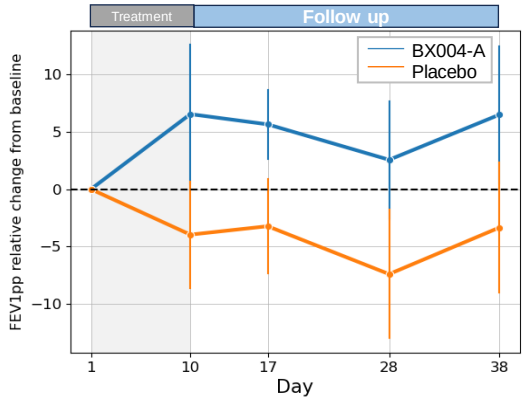


Figure 4: Relative FEV1 improvement in subjects on **continuous** inhaled antibiotics, on **ETI** and with **FEV1 <70%**

* *p*=0.22

During treatment, there were **no adverse events of special interest or serious adverse events** (in both Parts)

CONCLUSION

Phase 1b/2a clinical trial assessed safety, tolerability, and efficacy of BX004-A in CF subjects with chronic Pa pulmonary infection:

BX004-A showed **favorable safety** and **notable microbiologic and clinical efficacy**

Next steps

Phase 2b clinical trial planned

- Randomized, double-blind, placebo-controlled, multi-center study in approximately 60 patients with CF and chronic *P. aeruginosa* pulmonary infection
- Randomized 2:1 to BX004 or placebo as twice daily inhalation x 8 weeks

ACKNOWLEDGEMENTS

This work was supported by the Cystic Fibrosis Foundation (CFF) equity investment, and Israel Innovation Authority grants 74353, 77602, 80327

Thank you to CFF, TDN, ECFS-CTN for their support

A special Thank you to our entire BiomX team, all our subjects, investigators, site teams, Rho, Inc (our CRO), Jafral and other vendors, specialty laboratories and collaborators

Thank You!