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Late Breaking Abstract - A novel treatment for chronic P. 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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Pseudomonas aeruginosa (*PsA*), a major respiratory pathogen, poses a critical challenge in the care of cystic fibrosis (CF) patients due to its ability to cause chronic and difficult-to-treat infections, leading to a decline in lung function affecting longevity, increased hospitalizations, and decreased quality of life. Bacteriophage (phage) therapy offers a novel alternative or adjunct option to antibiotics in chronic *PsA* infections.

Objectives: This phase 1b/2a study aims to (1) assess safety and tolerability of nebulized phage (BX004-A) in patients with CF with chronic *PsA* pulmonary infection and (2) investigate the effects of nebulized phage (BX004-A) on reducing the level of *PsA* in sputum and effect on clinical outcomes.

Methods: A randomized, double-blind, placebo-controlled, multicenter study evaluating safety, tolerability, and efficacy of nebulized BX004-A on top of standard of care antibiotics in at least 32 patients with CF. Clinical *PsA* strain genomes were sequenced by next-generation sequencing.

Results: In Part 1, 9 subjects were randomized (7 on BX004-A, 2 on placebo). BX004-A was well-tolerated with no treatment-related adverse events. Mean PsA colony forming unit reduction at Day 15 (compared to baseline) was -1.42 log (BX004-A) vs. -0.28 log (placebo). Bacterial genomic analysis demonstrated that each patient was consistently colonized with the same genotypic strain of PsA, from Screening up to end of therapy. Part 2 is ongoing with similar baseline characteristics.

Conclusions: Part 1 results demonstrate that BX004-A was well-tolerated and showed notable bacterial reduction.