CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 20-0001
Study Title:

A Phase 1b/2, Multi-Centered, Randomized, Double-Blind, Placebo-Controlled Trial of the Safety and Microbiological Activity of a Single Dose of Bacteriophage Therapy in Cystic Fibrosis Subjects Colonized with *Pseudomonas aeruginosa*

NCT05453578

Version 1.0

DATE: 14 November 2023

RESTRICTED

STUDY TITLE

Protocol Number Code:	**DMID Protocol: 20-0001**
Development Phase:	Phase 1b/2
Products:	Bacteriophage (WRAIR-PAM-CF1 is a cocktail of four bacteriophages: PaWRA01Phi11, PaWRA01Phi39, PaWRA02Phi83, and PaWRA02Phi87)
Form/Route:	Intravenous (IV) Infusion
Indication Studied:	*Pseudomonas aeruginosa* respiratory colonization in adult Cystic Fibrosis (CF) subjects
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	03OCT2022
Clinical Trial Completion Date:	TBD
Date of the Analysis Plan:	14NOV2023
Version Number:	Version 1.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Classification
AUC	Area Under the Curve
BP	Blood Pressure
BPM	Beats Per Minute
BUN	Blood Urea Nitrogen
C	Celsius
CF	Cystic Fibrosis
CFQ-R	Cystic Fibrosis Questionnaire-Revised
CFRSD	Cystic Fibrosis Respiratory Symptom Diary
CFTR	Cystic Fibrosis Transmembrane Conductance Regulator
CFU	Colony Forming Units
CI	Confidence Interval
CM	Concomitant Medication
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
DMID	Division of Microbiology and Infectious Diseases
DOOR	Desirability of Outcome Ranking
DSMB	Data and Safety Monitoring Board
eCRF	Electronic Case Report Form
ESI	Event of Special Interest
ET	Early Termination
FEV1	Forced Expiratory Volume 1
FDA	Food and Drug Administration
GLI	Global Lung Function Initiative
HCG	Human Chorionic Gonadotropin
HLT	High Level Term

List of Abbreviations *(continued)*

ICF	Informed Consent Form
ICH	International Council for Harmonisation
IPW	Inverse Probability Weighting
IRB	Institutional Review Board
ITT	Intent-to-Treat
IV	Intravenous
IWRS	Interactive Web Response System
L	Liter
LLT	Lower Level Term
MAR	Missing at Random
mcg	Microgram
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
MIC	Minimum Inhibitory Concentration
mL	Milliliter
MOP	Manual of Procedures
N	Number (typically refers to subjects)
NIH	National Institutes of Health
ONR	Outside Normal Range
PFU	Plaque Forming Units
PID	Patient Identification
PIP	Predicted Interval Plot
PK	Pharmacokinetic
PST	Phage Susceptibility Testing
PT	Preferred Term
QoL	Quality of Life
qPCR	Quantitative Polymerase Chain Reaction
RBC	Red Blood Cell
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
SOC	System Organ Class

List of Abbreviations *(continued)*

TEAE	Treatment-Emergent Adverse Events
US	United States
USP	United States Pharmacopeia
WBC	White Blood Cell
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Phase 1b/2, Multi-Centered, Randomized, Double-Blind, Placebo-Controlled Trial of the Safety and Microbiological Activity of a Single Dose of Bacteriophage Therapy in Cystic Fibrosis Subjects Colonized with *Pseudomonas aeruginosa*" (Division of Microbiology and Infectious Diseases [DMID] Protocol 20-0001) describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, listings, and figures planned for the final analyses. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Council for Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials), Topic E6 (Good Clinical Practice), and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA) and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains: (1) a review of the study design, (2) general statistical considerations, (3) comprehensive statistical analysis methods for microbiological activity/benefit to risk profile and safety outcomes, and (4) a list of proposed tables and figures. Within the table, figure, and listing mock-ups (Appendices 1, 2, and 3), references to CSR sections are included. Any deviation from this SAP will be described and justified in protocol amendments and/or in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

This is a Phase 1b/2, multi-center, randomized, placebo-controlled, double-blind study of a single dose of intravenous (IV) bacteriophage in approximately 72 clinically stable adult cystic fibrosis (CF) subjects colonized with *Pseudomonas aeruginosa* (*P. aeruginosa*) in expectorated sputum. The study outcomes include safety and microbiological activity of IV bacteriophage therapy.

This study will include the following stages:

Stage 1 (Unblinded Safety Assessment/Dose-Escalation in Sentinel Subjects): Following screening, eligible subjects will be sequentially assigned to one of the three IV bacteriophage dosing regimens. A total of six sentinel subjects will be enrolled in Stage 1 of the study. Subjects will be sequentially enrolled with bacteriophage dose escalation by one $\log_{10}$ (starting at 4×10^7 plaque forming units (PFU), followed by 4×10^8 PFU, and 4×10^9 PFU). In each dosing arm, two subjects will be enrolled to serve as sentinels. Each sentinel subject will receive a single dose of IV bacteriophage therapy, followed by an observation period of 30 ± 7 days.

If no serious adverse events (SAEs) related to the study product are identified during the 96 hours after bacteriophage administration for all sentinel subjects in Stage 1, the study will proceed to Stage 2.

Stage 2 (Double-Blind Comparison): This stage consists of two parts, Stage 2a and Stage 2b. In Stage 2a, 32 subjects will be randomly assigned to one of the four arms: 4×10^7 PFU dose, 4×10^8 PFU dose, 4×10^9 PFU dose, or placebo in a 1:1:1:1 allocation. An interim analysis will be performed to determine the bacteriophage dosing with the most favorable safety and microbiologic activity profile. During Stage 2b, 24-34 subjects will be randomized into the bacteriophage (dose and sample size selected based on interim analysis following Stage 2a) or placebo arm.

2.1. Purpose of the Analyses

The analyses will assess the safety and microbiological activity of a single dose of IV bacteriophage therapy in comparison with placebo in clinically stable CF subjects with *P. aeruginosa* in expectorated sputum and will be included in the CSR.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary

- Describe the safety of a single dose of IV bacteriophage therapy in clinically stable CF subjects with *P. aeruginosa* in expectorated sputum.
- Describe the microbiological activity of a single dose of IV bacteriophage therapy in clinically stable CF subjects with *P. aeruginosa* in expectorated sputum.
- Describe the benefit to risk profile of a single dose of IV bacteriophage therapy in clinically stable CF subjects with *P. aeruginosa* in expectorated sputum.

3.1.2. Secondary

Not applicable.

3.1.3. Exploratory

- Characterize the serum and sputum pharmacokinetic (PK) profiles of a single dose of IV bacteriophage therapy in clinically stable CF subjects with *P. aeruginosa* in expectorated sputum.
- Describe changes in lung function from the administration of a single dose of IV bacteriophage therapy through Day 30 ± 7.
- Characterize geographically diverse *P. aeruginosa* isolates susceptibility to bacteriophages.
- Describe subjects' quality of life (QoL) before and after receiving bacteriophage therapy.

3.2. Endpoints

3.2.1. Primary

- Number of Grade 2 or higher treatment-emergent AEs through Day 30 ± 7.
- Change from baseline to Day 30 ± 7 in $\log_{10}$ *P. aeruginosa* total colony counts in quantitative sputum cultures after administration of IV bacteriophages/placebo.
- Desirability of Outcome Ranking (DOOR) using greatest reduction by Day 8 + 3 follow-up visit.

3.2.2. Secondary

Not applicable.

3.2.3. Exploratory

- Population mean PK parameter estimates and the magnitude of the associated inter-individual variability for IV bacteriophage therapy in serum and sputum.
- Individual post hoc PK parameter estimates and calculated exposure measures in serum for IV bacteriophage therapy.

- Individual post hoc PK parameter estimates and calculated exposure measures in sputum for IV bacteriophage therapy.
- Changes in the forced expiratory volume in 1 second (FEV1) from the administration of IV bacteriophages through Day 30 ± 7 days.
- Changes in $\log_{10}$ *P. aeruginosa* colony counts of each morphology in quantitative sputum cultures from administration of IV bacteriophages through Day 30 ± 7.
- Proportion of *P. aeruginosa* isolates susceptible to individual bacteriophages and the bacteriophage cocktail.
- Change from baseline through Day 30 ± 7 follow-up visit of QoL as measured with the Cystic Fibrosis Questionnaire-Revised (CFQ-R) and the Cystic Fibrosis Respiratory Symptom Diary (CFRSD).

3.3. Study Definitions and Derived Variables

3.3.1. Definitions for the DOOR Endpoint

Most desirable	Rank 1	No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL
↑	Rank 2	No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL
↓	Rank 3	No SAE (related to study product) and < 1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL
Least desirable	Rank 4	SAE (related to study product)
Abbreviations: CFU: colony-forming units; mL: milliliter; SAE: serious adverse events.		

3.3.2. Baseline

Baseline for all variables will be defined as the last measurement/laboratory value collected prior to dosing during the Baseline/Dosing Visit 2 (Day 1), unless otherwise noted.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a Phase 1b/2, multicenter, randomized, double-blind, placebo-controlled study of the safety and microbiological activity of a single dose of bacteriophage therapy in approximately 72 clinically stable adult CF subjects colonized with *P. aeruginosa*.

As part of screening, an expectorated sputum sample will be obtained from each subject and tested for the presence of *P. aeruginosa*. If *P. aeruginosa* is isolated from the sputum and all eligibility criteria are met, the subject will be eligible for the study. If *P. aeruginosa* is not isolated, the subject will be considered a screen failure. Screening for susceptibility of *P. aeruginosa* to the 4-component bacteriophage mixture will not occur prior to administration of study product.

The progression of subjects through the study is illustrated in Figure 2. This study will include the following three stages as shown in Figure 1.

Stage 1 (Unblinded Safety Assessment/Dose-Escalation in Sentinel Subjects): Following screening, eligible subjects will be sequentially assigned to one of the three IV bacteriophage dosing regimens. A total of six sentinel subjects will be enrolled in Stage 1 of the study. Subjects will be sequentially enrolled with bacteriophage dose escalation by one $\log_{10}$ (starting at 4×10^7 PFU, followed by 4×10^8 PFU, and 4×10^9 PFU). In each treatment group, two subjects will be enrolled to serve as sentinels. Each sentinel subject will receive a single dose of IV bacteriophage therapy, followed by an observation period of 30 ± 7 days.

If no SAEs (related to the study product) are identified during the 96 hours after bacteriophage administration for all Sentinel subjects in Stage 1, the study will proceed to Stage 2.

Stage 2 (Double-Blind Comparison): This stage consists of two parts, Stage 2a and Stage 2b. In Stage 2a, 32 subjects will be randomly assigned to one of the four treatment groups: 4×10^7 PFU dose, 4×10^8 PFU dose, 4×10^9 PFU dose, or placebo in a 1:1:1:1 allocation. The subjects and the protocol team will be blinded to bacteriophage versus placebo preparations. An interim analysis will be performed to determine the bacteriophage dosing with the most favorable safety and microbiologic activity profile. This will occur after eight subjects per arm have been randomized and completed their last follow-up visit. The interim analysis will use data from Stage 2a to identify the bacteriophage dose and the sample size that will be used for Stage 2b. During Stage 2b, 24-34 subjects will be randomized into the bacteriophage (dose selected based on interim analysis following Stage 2a) or placebo treatment group. If necessary, the sample size will be increased to up to 25 subjects in the placebo treatment group and up to 25 subjects in the selected dose for the bacteriophage treatment group.

The final sample size is expected to be up to 72 subjects.

A schedule of study procedures is available in Table 1. Detailed descriptions of each study visit can be found in Section 6 of the protocol.

4.2. Discussion of Study Design, Including the Choice of Control Groups

This clinical trial is designed to describe the safety and microbiologic activity of bacteriophages directed at *P. aeruginosa* in clinically stable CF subjects with *P. aeruginosa* respiratory colonization. This is a dose-ranging study of IV anti-pseudomonal bacteriophage therapy. Sentinel subjects will be enrolled first and receive a

single IV dose of a 4-component anti-pseudomonal bacteriophage (see Protocol Section 4.4 for details); all subjects must be monitored for the subsequent 96 hours (Stage 1) before enrollment in Stage 2 can begin.

Stage 1 subjects will continue to be monitored for 30 ± 7 days. After Stage 1 enrollment and the 96-hour monitoring period are complete, eligible subjects will be enrolled into Stage 2 and receive a single IV dose of a 4-component anti-pseudomonal bacteriophage or placebo. The subjects will then be monitored for 30 ± 7 days. Stage 2a will randomize subjects to placebo or one of three different doses of bacteriophage. After the last Stage 2a subject has completed his/her last study visit, study enrollment will be held for an interim analysis to determine the dose that will be used in Stage 2b. This trial will limit the route of administration of bacteriophages to the IV route. As the safest, yet still microbiologically active dosage of bacteriophages has yet to be defined, this will be a dose-ranging study evaluating approximately 1 x 10^7 PFU, 1 x 10^8 PFU, and 1 x 10^9 PFU of each bacteriophage (equaling a total of 4 x 10^7 PFU, 4 x 10^8 PFU, and 4 x 10^9 PFU of bacteriophages in the 4-component bacteriophage mixture). It is expected that a single dose of bacteriophage will be safe and lead to at least a one-$\log_{10}$ decrease in *P. aeruginosa* colony forming unit (CFU)/milliliter (mL) in sputum, compared to baseline.

4.3. Selection of Study Population

This is a Phase 1b/2 clinical trial that will enroll up to 72 CF subjects. Clinically stable volunteers will be recruited from up to 20 CF outpatient clinics in the United States (US). All study visits will occur in the ambulatory setting. There will be no enrollment from international sites. A detailed review of the study will be discussed with potential subjects and written consent will be obtained prior to enrollment. Inclusion will be limited to subjects 18 years of age or older (at the time of the screening) who are capable of providing informed consent. Furthermore, subjects should be capable and willing to complete all study visits and perform all procedures required by the protocol. Individuals who are pregnant, planning to become pregnant at any time during the study period, or breastfeeding will not be included as the impact of bacteriophage therapy on pregnancy, fetuses, and neonates is unknown. Cystic fibrosis primarily affects persons of European backgrounds and generally has an unequal distribution across races and ethnicities. It is expected that the racial and ethnic distribution of enrolled subjects will reflect those of the local CF communities from where subjects are recruited but may not reflect the US population as a whole. Prisoners and other potentially vulnerable populations will not be enrolled.

Subject inclusion and exclusion criteria must be confirmed by a study investigator listed on the Form FDA 1572. No exemptions are granted on Subject inclusion/exclusion Criteria in DMID-sponsored studies. Clarifications regarding applicability of specific inclusion and exclusion criteria may be discussed with the study investigator. Questions about eligibility will also be directed toward the DMID Medical Officer.

4.3.1. Inclusion Criteria

Refer the most recent version of the protocol for a list of the inclusion criteria.

4.3.2. Exclusion Criteria

Refer the most recent version of the protocol for a list of the exclusion criteria. .

4.3.3. Withdrawal from the Study or Discontinuation of the Study Product

Subjects may voluntarily withdraw their consent for study participation at any time without penalty or loss of benefits to which they are otherwise entitled. An investigator may also withdraw a subject from receiving the study product for any reason. Follow-up safety evaluations will be conducted if the subject agrees. If a subject withdraws or is withdrawn prior to completion of the study, the reason for this decision must be recorded in the case report forms (CRFs). The reasons, might include, but are not limited to the following:

- Subject no longer meets eligibility criteria
- Subject meets individual halting criteria (refer to the protocol, Section 8.6.2)
- Subject becomes noncompliant
- Medical disease or condition, or new clinical finding(s) for which continued participation, in the opinion of the investigator, might compromise the safety of the subject, interfere with the subject's successful completion of this study, or interfere with the evaluation of responses
- Subject lost to follow-up
- Determined by the investigator's discretion to require additional therapy not indicated in the protocol to ensure subject's health and well-being (or treatment failure, if applicable)

The investigator should be explicit regarding study follow-up (e.g., safety follow-up) that might be carried out despite the fact that the subject will not receive further study product. If the subject consents, every attempt will be made to follow all AEs through the study defined follow-up period, and all SAEs through resolution. The procedures that collect safety data for the purposes of research must be inclusive in the original informed consent or the investigator may seek subsequent informed consent using an Institutional Review Board (IRB) -approved consent form with the revised procedures.

The investigator will inform the subject that already collected data will be retained and analyzed even if the subject withdraws from this study.

4.3.4. Subject Replacement

Subjects who withdraw, are withdrawn from this study, or are lost to follow-up after signing the Informed Consent Form (ICF) and administration of the study product, will not be replaced. Subjects who withdraw, are withdrawn from this study, or are lost to follow-up after signing the ICF, but prior to administration of study product, may be replaced.

4.3.5. Study Termination

If the study is prematurely terminated by the sponsor, any regulatory authority, or the investigator for any reason, the investigator will promptly inform the study subjects and assure appropriate therapy or follow-up for the subjects, as necessary. The investigator will provide a detailed written explanation of the termination to the IRB.

4.4. Treatments

4.4.1. Treatments Administered

Subjects will receive either a 4×10^7 PFU, 4×10^8 PFU, or 4×10^9 PFU dose of IV bacteriophage or placebo according to study stage as described in Figure 1.

Bacteriophage should be thawed at room temperature and diluted in normal saline to a final administration volume of 25 mL. The final dilution will be administered as a 30 (± 15-35 minutes) minute IV infusion. Placebo will be normal saline at a final volume of 25 mL and administered as a 30 (± 15-35 minutes) minute IV infusion. A saline flush will occur after administration of study product or placebo. Collection times for samples will be based on the completion time of the IV flush.

4.4.2. Identity of Investigational Product(s)

Bacteriophage

The bacteriophage was packaged in two mL vials. Each vial will contain 1 mL of a single bacteriophage at a concentration of 1 x 10^9 to 1 x 10^{11} PFU/mL suspended in PlasmaLyte A and 20% (v/v) of glycerol. Bacteriophage is a clear to slightly turbid suspension, essentially free of foreign particulates. The bacteriophage was labeled according to manufacturer specifications and regulatory requirements and include the statement "Caution: New Drug – Limited by Federal Law to Investigational Use." Additional label contents are detailed in the protocol-specific Manual of Procedures (MOP).

The 4-component bacteriophage mixture will include a 1:1:1:1 combination of four individual bacteriophage (refer to the protocol, Table 2) and will contain a total of 4 x 10^7 PFU, 4 x 10^8 PFU, or 4 x 10^9 PFU, depending on the target dose. The final bacteriophage combination to be administered to each subject will be diluted to the target dose with normal saline. Dosing will be based on the actual product potency, according to instructions that will be provided in the MOP, which will be updated as necessary, based on the most recent potency results.

Placebo (Normal Saline, 0.9% Sodium Chloride, US Pharmacopeia [USP])

For the placebo, 0.9% Sodium Chloride Injection, USP, is a sterile, nonpyrogenic, isotonic solution of sodium chloride and water for injection. Each mL contains 9 milligram (mg) of sodium chloride and no preservatives, antimicrobial agents, or added buffer. The solution is clear in appearance with a pH range of 4.5 to 7.0. Normal saline used for the placebo will be supplied in pre-filled infusion bags. Each infusion bag should only be used for one dosing preparation.

The placebo will be labeled according to manufacturer specifications and regulatory requirements and include the statement "Caution: New Drug – Limited by Federal Law to Investigational Use." Additional label contents are detailed in the protocol-specific MOP.

4.4.3. Method of Assigning Subjects to Treatment Groups (Randomization)

The randomization scheme will be generated and maintained by The Emmes Company, LLC (Emmes). Subjects will be randomized using the Emmes Interactive Web Response System (IWRS).

In Stage 1, two sentinel subjects will each be sequentially assigned to one of three IV bacteriophage doses: 4 x 10^7 PFU, 4 x 10^8 PFU, or 4 x 10^9 PFU. Randomization for Stage 2a and Stage 2b will be performed using a permuted block design, where each site will receive a treatment table accounting for all enrolled study subjects. In Stage 2a, 32 subjects will be randomly assigned to receive one of three IV bacteriophage doses or placebo in a ratio of 1:1:1:1. In Stage 2b, 24-34 subjects will be assigned to either the selected IV bacteriophage dose, selected from the interim analysis results, or placebo in a ratio of 1:1.

4.4.4. Selection of Doses in the Study

The minimum and maximum doses that are being investigated in this study were informed by previous case reports, case series, and clinical trials, which generally used IV doses ranging from approximately 10^7 PFU to 10^{10} PFU (refer to the protocol, Table 1). A single dose is being administered in order to evaluate the safety of the 4-component bacteriophage product prior to moving to a multi-dose regimen.

4.4.5. Selection and Timing of Dose for Each Subject

Subjects will receive a single 30 (± 15-35 minutes) minute IV infusion of bacteriophage or placebo. Sentinel subjects in Stage 1 will be monitored for SAEs for 96 hours after dosing. After Stage 1 enrollment and the 96-hour monitoring period are complete, eligible subjects will be enrolled into Stage 2a and Stage 2b to receive a single IV dose of a 4-component bacteriophage or placebo. The interim analysis will use data from Stage 2a to identify the bacteriophage dose and the sample size that will be used for Stage 2b. For more information regarding selection of dose amounts, refer to Section 4.4.4.

4.4.6. Blinding

Stage 1 of the study will not be blinded.

A double-blind/masking technique will be used in Stage 2 of the study. The three IV bacteriophage doses and placebo will be packaged identically so that treatment blind/masking is maintained. The subject and the investigator or delegate(s) who are involved in the treatment or clinical evaluation of the subjects will be unaware of the treatment group assignments. To maintain the overall quality and legitimacy of the clinical trial, randomization code breaks should occur only in exceptional circumstances when knowledge of the actual treatment is absolutely essential for further management of the subject. Investigators are encouraged to discuss with study team if he/she believes that unblinding is necessary. Information on laboratory blinding procedures is available in the MOP.

Emergency unblinding of treatment assignment for a subject may be necessary due to a medical emergency or other significant medical events. Procedures for emergency unblinding are detailed in the MOP. The treatment assignment code list will be kept in a secure place at all times at the responsibility of the Statistical and Data Coordinating Center (SDCC), at Emmes.

4.4.7. Prior and Concomitant Therapy

Any systemic medication taken by the subject, other than study drugs, is considered a concomitant medication. All concomitant medications from Screening (Visit 1) through Day 30 ± 7 (Visit 7) must be recorded in the subject's medical record and on the electronic case report forms (eCRFs).

If a subject is prescribed antibiotic therapy with activity against *P. aeruginosa* after receipt of the study product, the subject will continue in the study and be included in an intent-to-treat (ITT) analysis. Receipt of antibiotic therapy with activity against *P. aeruginosa* will be documented as a concomitant medication and the underlying condition for which the antibiotics were taken will be reported as an AE.

4.4.8. Treatment Compliance

Subjects will be directly observed while receiving a single dose of study product or placebo by a member of the study team who is licensed to administer the study product or placebo. Administration data will be recorded in the source and entered into the eCRF.

4.5. Primary Endpoint Variables

The three primary objectives are as follows: (1) the safety of a single dose of IV bacteriophage therapy in clinically stable CF subjects with *P. aeruginosa* in expectorated sputum, (2) the microbiological activity of a single dose of IV bacteriophage therapy in clinically stable CF subjects with *P. aeruginosa* in expectorated sputum, and (3) the benefit to risk profile of a single dose of IV bacteriophage therapy in clinically stable CF subjects with *P. aeruginosa* in expectorated sputum.

The safety endpoint will be measured by the number of Grade 2 or higher treatment-emergent AEs through Day 30 ± 7. Safety will also be assessed through the incidence of treatment-emergent adverse events (TEAEs), on-therapy SAEs, and AEs leading to premature discontinuation. Adverse events will be graded according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0, November 2017 (https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm#ctc_50). Details about adverse event grading and determination of relationship to study product can be found in the protocol, Section 8.1.1.1.

Clinical laboratory results, including chemistry, hematology, and liver function tests, will also be graded according to the CTCAE scale. Clinical chemistry parameters include serum creatinine, blood urea nitrogen (BUN), glucose, sodium, potassium, chloride, bicarbonate, and calcium. Hematology parameters include complete blood count with red blood cell (RBC) count, hemoglobin, hematocrit, total white blood cell (WBC) count with differential counts, and platelet count. Liver function tests include aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, total bilirubin, lactate dehydrogenase, albumin, and total protein. Only AST, ALT, and total bilirubin are collected at Screening. Clinical chemistry, hematology, and liver function tests will be performed at baseline and at follow-up visits occurring on Days 2, 5, 8, 12 (Stage 1 only), and 30. Refer to Section 3.3.2 for the definition of baseline.

The microbiological activity endpoint will be measured based on the change in $\log_{10}$ *P. aeruginosa* colony counts after administration of IV bacteriophages/placebo. Sputum collection for measuring colony counts will occur at baseline and at follow-up visits occurring on Days 2, 5, 8, and 30.

Finally, DOOR will be used to describe the benefit to risk profile based on the greatest reduction in DOOR category by the Day 8 + 3 follow-up visit. DOOR is a composite endpoint which includes whether or not a subject experienced an SAE (related to study product) and what category their reduction in *P. aeruginosa* colony counts falls into; >2 $\log_{10}$ reduction in CFU/mL, 1-2 $\log_{10}$ reduction in CFU/mL, or <1 $\log_{10}$ reduction in CFU/mL.

4.6. Exploratory Endpoint Variables

There will be four exploratory objectives: (1) characterize the serum and sputum PK profiles of a single dose of IV bacteriophage therapy in clinically stable CF subjects with *P. aeruginosa* in expectorated sputum, (2) change in lung function from the administration of a single dose of IV bacteriophage therapy through Day 30 ± 7, (3) characterize geographically diverse *P. aeruginosa* isolates susceptibility to bacteriophages, and (4) describe subjects' QoL before and after receiving bacteriophages. The SAP for the first exploratory objective, related to serum and sputum PK, will be provided in a separate document.

Change in lung function will be measured using FEV1. Spirometry will be performed at screening, baseline, and at follow-up visits occurring on Days 2, 5, 12, and 30.

Phage susceptibility testing (PST) will occur using a plaque assay and the liquid assay. These assays describe the proportion of *P. aeruginosa* isolates that are susceptible to each phage and to the phage cocktail. Both the plaque assay and liquid assay will be evaluated every time sputum is obtained (see schedule of study

procedures in Table 1). An isolate will be considered susceptible to phage if both the plaque assay and the liquid assay indicate susceptibility.

The CFQ-R (https://cfqr-app.netlify.app/#/questionnaire) is a self-administered QoL questionnaire designed to measure the impact that CF has on overall health, daily life, and perceived well-being and symptoms. The CFQ-R contains 50 items and will be administered at in-person and virtual study visits for Stage 2 subjects. The CFRSD (https://depts.washington.edu/seaqol/CFRSD-CRISS) is a subject reported outcome measure that is used to evaluate the effect of treatment on respiratory infection symptom severity in patients with CF and chronic respiratory infection. Quality of Life will be measured using the CFQ-R and the CFRSD. The CFQ-R will be administered at baseline and at the final follow-up visit (Day 30 ± 7). The CFRSD will be administered at baseline and at follow-up visits occurring on Day 2, 5, 8, and 30.

5. SAMPLE SIZE CONSIDERATIONS

The sample size for Stage 2 (Stage 2a/2b) was determined using DOOR. The sample size was calculated to provide desired precision of the estimate of the DOOR probability in order to describe the benefit to risk profile of a single dose of IV bacteriophage in clinically stable CF subjects with *P. aeruginosa* in expectorated sputum. If the true DOOR probability comparing IV bacteriophage and placebo is 70%, when the total sample size in each arm is 20-25 (combining subjects from Stages 2a and 2b), the two-sided normal approximate 95% confidence interval (CI) for DOOR probability is calculated at 51% and 89%, respectively, with the lower limit larger than 50%.

An interim analysis will be performed when the eight subjects per arm in Stage 2a (40% = 8/20) have completed the follow-up through their last follow-up visit, which will be Day 30 ± 7 if they complete all follow-up visits. Only a single dosage of IV bacteriophage therapy to be used in Stage 2b will be determined during the interim analysis and the planned sample size will be re-evaluated to whether it provides the desired precision of estimates of the DOOR probability for a selected dose and placebo. If necessary, after completion of Stage 2a and per details in Section 6.6, the sample size will be increased up to 17 subjects for each of the two arms in Stage 2b (a total of up to 25 for the placebo arm and up to 25 for the selected bacteriophage dose in Stage 2).

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

All continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation (SD), median, quartiles, maximum, and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures. In general, all data will be listed, sorted by treatment and subject, and when appropriate by visit number within subject.

All safety summary tables and figures will be summarized by the following treatment groups in the following order:

- 4×10^7 PFU dose
- 4×10^8 PFU dose
- 4×10^9 PFU dose
- Placebo

The safety analysis in this SAP will include subjects from Stage 1, Stage 2a, and Stage 2b.

All microbiological activity and benefit to risk analyses, including the interim analysis, will be summarized by the following treatment groups in the following order:

- IV Bacteriophage Selected Dose
- Placebo

with "IV Bacteriophage Selected Dose" being replaced with the selected IV Bacteriophage dose found in the interim analysis, described in Section 8.3. The 'IV Bacteriophage Selected Dose' group will include subjects from Stage 2a and Stage 2b who received the selected IV bacteriophage dose. The 'Placebo' group will include subjects from Stage 2a and Stage 2b who received the placebo.

6.2. Timing of Analyses

There will be one planned interim analysis of the primary endpoints after all randomized subjects for Stage 2a have completed follow-up through Day 30 ± 7 or the last study visit for those who withdrew early. Enrollment will be held until the dose for Stage 2b is determined from the planned interim analysis. More details regarding the interim analysis can be found in Section 6.6.

The Data and Safety Monitoring Board (DSMB) will evaluate safety at pre-specified intervals; however, ongoing review and summary of subjects' safety will occur to allow for early detection of a safety signal that may result from an AE. The DSMB will advise the trial sponsor on whether to continue, modify, or terminate the trial based on risk assessment.

The final analysis will be performed after database lock.

6.3. Analysis Populations

The primary analysis will be performed using the ITT Population.

Reasons for exclusion from the screened analysis population are summarized in Table 10, Table 11, and Table 12, while reasons for exclusions from the rest of the analysis populations (ITT, Safety, PK) are summarized in Table 8 by treatment group. Individual subject listing of exclusion reasons is also provided in Listing 5. Excluded subjects might satisfy multiple criteria justifying their exclusion but will have only one reason indicated in Table 8 and Listing 5. The exclusion reason indicated will be determined by first exclusion reason met based on the following rules in the order they are listed for each analysis population.

6.3.1. Screened Population

The screened population will consist of all subjects who undergo the Screening Visit and receive a patient identification (PID) number.

6.3.2. Intent-to-Treat (ITT) Population

The ITT Population will consist of all randomized subjects regardless of whether or not they receive study product or placebo. ITT analysis will be performed based on the treatment that a subject is randomized to receive.

6.3.3. Safety Population

The Safety Population will consist of all randomized subjects who will receive at least some amount of study product or placebo. Subjects will be analyzed based on the treatment received.

6.3.4. Pharmacokinetics (PK) Population

The PK Population will consist of all randomized subjects who will contribute at least two samples each of sputum and blood.

6.4. Covariates and Subgroups

An exploratory analysis of the primary outcomes will be conducted to explore whether estimated treatment effects vary significantly between subcategories of trial subjects. Bacteriophage susceptibility will be the only pre-specified subgroup analyzed, however exploratory analyses of the primary endpoints may be performed using any other subgroups of interest.

6.5. Missing Data

While all efforts will be made to minimize missing data, some missing data is expected. Whenever possible, subjects terminating from the study early will be given an early termination (ET) visit during which the available components of DOOR and related measures can be recorded. A sensitivity analysis of DOOR will be performed using inverse probability weighting (IPW) to reduce the bias in DOOR outcome caused by missing data, assuming a missing at random (MAR) model (see Section 8.1.3.1). No other endpoints will be analyzed using techniques for missing data.

The effect that any missing data might have on results will be assessed via the inclusion of the IPW sensitivity analysis.

6.6. Interim Analyses and Data Monitoring

An interim analysis will be performed when all randomized subjects for Stage 2a have completed follow-up, through Day 30 ± 7, or the last study visit for those who withdrew early.

The purpose of the interim analysis will be to select one IV bacteriophage dose with the most favorable benefit to risk profile compared to placebo for further evaluation in Stage 2b. The interim analysis will also serve to exclude proceeding with bacteriophage doses that are associated with safety issues, do not reduce pseudomonal colony counts, or have low conditional power. An independent statistician at the SDCC will report to the Phage Advisory Group. The Phage Advisory Group will make a recommendation to the DMID on the selected dose to be considered for Stage 2b. This will only be a recommendation. Ultimately, DMID will review the recommendation (as well as the DSMB recommendation based on independent review of safety and microbiological activity data) and make the final decision on how to proceed regarding Stage 2b.

The interim analysis will consist of a quantitative evaluation of potential effect sizes and associated precision using predicted intervals and predicted interval plots (PIPs) approach. Predicted intervals for DOOR probability will be calculated under the range of assumptions outlined in Section 8.3.

By relying on prediction intervals, no statistical hypothesis testing is required, and no power is lost at interim analysis [1]. In addition, as supplementary information, (predictive) conditional power will be calculated to quantify the probability of rejecting the null hypothesis at the final analysis under a range of assumptions, which are listed in Section 8.3.

Similar to DOOR, changes in $\log_{10}$ *P. aeruginosa* colony counts (total and each morphology) in sputum cultures from administration of IV bacteriophages through Day 8 + 3, will be evaluated using PIPs to assess the precision for measuring differences in $\log_{10}$ CFU/mL count.

The planned sample size (20 subjects per Stage 2b arm) will be reevaluated after completion of Stage 2a. If necessary, the sample size will be increased up to 25 subjects for the two arms in Stage 2b (up to 25 subjects for the placebo arm and up to 25 subjects for the selected bacteriophage dose) to provide the desired precision of estimates.

Details of the interim analysis are provided in Section 8.3.

6.7. Multicenter Studies

This is a multicenter study, but randomization is not stratified by site. Data will be pooled across all clinical sites and analyses will not adjust for potential site effects.

6.8. Multiple Comparisons/Multiplicity

This exploratory study does not include formal hypothesis testing for any of the primary endpoints, therefore no adjustments for multiple testing are planned.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

Reasons for screening failures will be summarized in Table 10 for Stage 1, Table 11 for Stage 2a, and Table 12 for Stage 2a and 2b. The number and percentage of subjects who complete the treatment period and study milestones, and of subjects who prematurely discontinue during the same period will be presented by treatment group for the ITT population in Table 5 and for the Safety Population in Table 6. The number and percentage of subjects who complete the treatment period and study milestones, and of subjects who prematurely discontinue during the same period will be presented by site for the screened population in Table 7. Enrolled subjects who were ineligible for inclusion in analysis populations will be summarized by reason for subject exclusion and treatment group in Table 8. A listing of subjects excluded from each analysis population and reason for exclusion will be presented in Listing 5.

Reasons for ET as recorded on the termination pages of the eCRF will be summarized (number and percentage) by treatment groups for the safety population in Table 13. Early terminations or discontinued subjects are presented in Listing 2.

Subject disposition and eligibility for analysis will be summarized in a Consolidated Standards of Reporting Trials (CONSORT) flow diagram (Figure 3 and Figure 4).

7.2. Protocol Deviations

A summary of subject-specific protocol deviations will be presented by the reason for the deviation, the deviation category, and treatment group for all enrolled subjects in Stage 1 in Table 2, Stage 2a in Table 3 and Stage 2a and 2b in Table 4. All subject-specific protocol deviations and non-subject specific protocol deviations will be included in Appendix 3 as data listings (Listing 3 and Listing 4, respectively).

Any missing CFQ-R or CFRSD assessments will not be considered protocol deviations. If an unscheduled study visit occurs, any assessments/procedures that do not occur will not be considered protocol deviations.

8. MICROBIOLOGICAL ACTIVITY AND BENEFIT TO RISK PROFILE EVALUATION

All variables in the microbiological activity and benefit to risk profile analyses will be listed by subject. Data will be summarized by treatment group. Continuous variables will be summarized with the number of observations, mean, median, SD, quartiles, minimum, and maximum. Categorical variables will be summarized by number and percent in each category. All microbiological activity and benefit to risk profile analyses will be performed using the ITT population.

This study does not include formal hypothesis testing for any of the primary endpoints, and instead relies on CIs for conclusions of treatment effects.

All microbiological activity and benefit to risk profile tables and figures will compare all subjects receiving placebo to all subjects receiving the selected dose of IV bacteriophage chosen from the interim analysis.

8.1. Primary Analysis

8.1.1. Safety Analysis

An event that occurs during the treatment period will be considered a TEAE if it was not present before the first dose of the study product or was present before the first dose of the study product and increased in severity during the treatment period.

The number of Grade 2 or higher TEAEs will be presented by Medical Dictionary for Regulatory Activities (MedDRA®) System Organ Class (SOC), High Level Term (HLT), and Preferred Term (PT) by treatment group in Table 44. Subjects will only be counted once for each SOC and PT. The difference in proportion of the number of subjects with events between the Selected dose IV bacteriophage and placebo arms with the corresponding exact 95% CI will be presented in Table 45. This is a primary endpoint and will be analyzed using the ITT population.

8.1.2. Microbiological Activity Analysis

Changes in *P. aeruginosa* CFU/mL in quantitative sputum cultures through Day 30 ± 7 and the corresponding 95% CI for the change from baseline will be summarized by treatment group in Table 19 and changes in $\log_{10}$ *P. aeruginosa* CFU/mL will be summarized in Table 20. The difference in $\log_{10}$-transformed and original scale mean change in *P. aeruginosa* colony counts between IV bacteriophage and placebo arms, along with the corresponding 95% CIs, will be presented in Table 21. A forest plot of the differences in *P. aeruginosa* colony counts is presented in Figure 6 and a forest plot of the differences in $\log_{10}$ *P. aeruginosa* colony counts is presented in Figure 7. The area under the curve (AUC) calculated using the trapezoidal rule will be used to summarize $\log_{10}$ *P. aeruginosa* CFU/mL over time. Linear trapezoidal rule will be used to calculate AUC. Area under the curve will only be calculated for subjects with non-missing colony count data from baseline through Day 30. Area under the curve of $\log_{10}$ *P. aeruginosa* CFU/mL colony counts by treatment group will be presented in Table 23. The difference in AUC between IV bacteriophage and placebo arms and the corresponding 95% CI will be calculated in Table 24. The 95% CI will be obtained from Welch's t-test.

A boxplot including the median, 25th percentile, and 75th percentile of colony counts over time by treatment group will be presented in Figure 5. A listing of individual colony counts will be presented in Listing 10 and a listing of *P. aeruginosa* morphotypes results will be presented in Listing 11.

8.1.3. Benefit to Risk Profile Analysis Using DOOR

Each subject will have a composite DOOR rank assigned to them based on the presence or absence of SAEs related to study product and the reduction in $\log_{10}$ *P. aeruginosa* CFU/mL. DOOR rank will be determined according to the definition in Section 3.3.1.

DOOR probability, which is defined by:

$$DOOR\ probability = Pr[DOOR_2 > DOOR_1] + \tfrac{1}{2} Pr[DOOR_2 = DOOR_1],$$

will be estimated using the Wilcoxon-Mann-Whitney statistic, correcting for ties and divided by the product of the placebo and IV bacteriophage group sample sizes, where

- $DOOR_2$ and $DOOR_1$ are the DOOR for IV bacteriophage and placebo arms, respectively
- $Pr[DOOR_2 > DOOR_1]$ is the probability of a DOOR from IV bacteriophage dose being more desirable than a DOOR from placebo, and
- $Pr[DOOR_2 = DOOR_1]$ is the probability that the DOOR outcomes in IV bacteriophage and placebo are the same.

The corresponding two-sided 95% CI will be calculated using the method described in Halperin et al. [2] for the incorporation of IPW described in Section 8.1.3.1. Note that all CIs are two-sided.

The 95% CI by Halperin et al. [2] will be calculated in the following manner:

- n_1: number of subjects in ITT population randomized to placebo
- n_2: number of subjects in ITT population randomized to IV bacteriophage
- W: Wilcoxon-Mann-Whitney statistic for ordinal outcomes, corrected for ties
- ζ: DOOR probability
- $\hat{\zeta}$: An unbiased estimator of ζ, $\hat{\zeta} = W/(n_1 n_2)$
- V: The variance of the DOOR probability. Correcting for ties, the formula for the variance of the DOOR Probability, as described in Halperin et al. [2], is:

$$\hat{V} = Var(\zeta) = \frac{1}{n_1 n_2}[n_1 + n_2 + 1 - (n_1 + n_2 - 2)\theta]\zeta(1-\zeta)$$

where

$$\theta = \frac{[(n_1 + n_2 - 2)\zeta - (n_2 - 1)A - (n_1 - 1)B]}{(n_1 + n_2 - 2)\zeta(1-\zeta)}$$

To obtain an estimator $\hat{\theta}$ of θ, the following formulas will be used for A and B, respectively:

$$\hat{A} = \hat{A}_1 - \frac{1}{n_2 - 1}\sum_{i=1}^{D-1} p_{1i}\left[q_{2i}\sum_{j=i+1}^{D} p_{2j} - \left(\sum_{j=i+1}^{D} p_{2j}\right)^2\right] - \frac{1}{4(n_2 - 1)}\sum_{i=1}^{D} p_{1i}p_{2i}q_{2i}$$

where

$$\hat{A}_1 = \sum_{i=1}^{D-1} p_{1i}\left[\sum_{j=i+1}^{D} p_{2j} + \frac{p_{2i}}{2}\right]^2 + \frac{p_{1D}p_{2D}^2}{4}$$

and

$$\hat{B} = \hat{B}_1 - \frac{1}{n_1 - 1}\sum_{j=2}^{D} p_{2j}\left[q_{1j}\sum_{i=1}^{j-1} p_{1i} - \left(\sum_{i=1}^{j-1} p_{1i}\right)^2\right] - \frac{1}{4(n_1 - 1)}\sum_{j=1}^{D} p_{2i}p_{1i}q_{1i}$$

where

$$\hat{B}_1 = \sum_{j=2}^{D} p_{2j}\left[\sum_{i=1}^{j-1} p_{1i} + \frac{p_{1j}}{2}\right]^2 + \frac{p_{11}^2 p_{21}}{4}$$

In the equations for A and B above, D is the number of DOOR outcome ranks in the dataset; p_{1i}, for i = 1, 2, …, D, represents the proportion of subjects randomized to placebo with the ith rank category of DOOR; p_{2j}, for i= 1, 2, … D, represents the proportion of subjects randomized to IV Bacteriophage with the jth value of DOOR; and q = 1 – p in general.

Additionally, the equation for an unbiased estimate of $\zeta(1-\zeta)$ is given by:

$$\frac{(n_1 n_2 - n_1 - n_2 + 2)\hat{\zeta} - n_1 n_2 \hat{\zeta}^2}{(n_1 - 1)(n_2 - 1)} + \frac{\hat{A}}{n_1 - 1} + \frac{\hat{B}}{n_2 - 1}$$

After substituting the values of A, B and $\zeta(1-\zeta)$ in the equation θ to obtain an estimate $\hat{\theta}$ of θ, θ is defined as follows: If $\hat{\theta} < 0$ then $\theta = 0$, if $\hat{\theta} > 1$ then $\theta = 1$, otherwise $\hat{\theta} = \theta$.

We now compute the pivotal quantity $Z_H{}^2 = (\hat{\zeta} - \zeta)^2/\hat{V}$.

$\gamma = (n_1 + n_2 - 1) - (n_1 + n_2 - 2)\hat{\theta}$

The CI is obtained as the solution set in ζ of the quadratic inequality:

$$n_1 n_2 \frac{(\hat{\zeta} - \zeta)^2}{\gamma\zeta(1-\zeta)} \leq \chi^2(1, 1-\alpha)$$

Let, $C = \gamma\chi^2(1, 1-\alpha)/(n_1 n_2)$. The CI is given as:

$$\frac{C + 2\hat{\zeta} \pm [C^2 + 4C\hat{\zeta}(1-\hat{\zeta})]^{1/2}}{2(C+1)}$$

The superiority of IV bacteriophage vs placebo is concluded if the lower bound of the 95% CI for the DOOR probability is larger than 50%.

Due to the presence of missing data, IPW will be used to handle missing data. For the sensitivity analysis of DOOR, IPW method will be used (see Section 8.1.3.1).

The DOOR will be analyzed as follows:

- DOOR probability with corresponding 95% CI calculated using the method described in Halperin et al. [2] calculated using the greatest reduction in *P. aeruginosa* CFU/mL by Day 8 (Table 26).
- DOOR categories distribution by treatment group through Day 8 + 3 (Table 28).

- Cumulative proportions of DOOR categories through Day 8 + 3 for IV bacteriophage vs. placebo with cumulative DOOR probabilities and corresponding 95% CI (Table 31). This analysis compares the DOOR probability from the following dichotomizations of DOOR: first by calculating the dichotomized DOOR probability comparing those with DOOR rank = 1 to DOOR ranks 2, 3, and 4 pooled together, then DOOR rank 1 and 2 compared to DOOR rank 3 and 4, and finally comparing DOOR ranks 1, 2, and 3 to DOOR rank 4.
- Sequential dichotomization of DOOR will be presented in Figure 12. Cumulative probabilities will be calculated using the following dichotomizations: rank 1 vs ranks 2, 3, and 4; ranks 1 and 2 vs ranks 3 and 4; and ranks 1, 2, and 3 vs rank 4.
- Comparison of each of the components of the DOOR between the IV bacteriophage and placebo arms through Day 8 with 95% CI, summarized by DOOR probability and 95% CI (Table 33). For the SAE component of DOOR the dichotomized DOOR probability will be calculated using 'No SAE' = rank 1 and 'SAE' = rank 2. For the log10 reduction component of DOOR the dichotomized DOOR probability will be calculated using '>2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL' = rank 1, '1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL' = rank 2, and '<1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL' = rank 3.
- Forest plot of probabilities of DOOR and its components at Day 8 + 3 and corresponding 95% CI calculated using the method in Halperin et. al. [2] (Figure 10).
- Point estimate and CI of difference in mean partial credit vs. placebo through Day 8 and corresponding 95% CI (Table 32). The 95% CI will be calculated using Welch's t-test. The partial credit analysis will be calculated assigning a grading key to each of the DOOR categories. The grading keys used will be the following: A: (DOOR rank 1 = 100, rank 2 = 100, rank 3 = 100, rank 4 = 0), B: (rank 1 = 100, rank 2 = 100, rank 3 = 0, rank 4 = 0), C: (rank 1 = 100, rank 2 = 0, rank 3 = 0, rank 4 = 0). For each scenario, the mean and SD of these partial credit scores will be provided for each treatment group and corresponding scenario.
- Difference in means of partial credit score by time point (Figure 13).

A listing of individual DOOR response data will be presented in Listing 12.

8.1.3.1. Intention-to-Treat (ITT) Analysis of DOOR using Inverse Probability Weighting

Intention-to-treat analysis requires that all randomized subjects be included in the analysis. However, missing data is prone to happen in clinical trials due to missing scheduled visits or loss to follow-up for example. In this case, analysis that is only based on complete data may be biased if the excluded subjects are systematically different from those included. IPW is one approach commonly used to reduce this bias under a MAR assumption. This is achieved by weighting complete cases with the inverse of their probability of being a complete case. While subjects missing the DOOR are excluded from the analysis per se, they may still inform the fitting of the logistic regression model used to provide predictions of the probability of completeness which are used to calculate the weights.

Specifically, let Y_i represent the outcome of interest (DOOR), X_i represent the covariates of interest, Z_i represent any other variables measured in the data but not used in the analysis model. For the IPW approach, we first define the missingness model to estimate the weights (w_i) using a logistic regression model with outcome L and covariates taken from set (X, Z) where L_i is defined as 1 if DOOR data is complete (not missing) and 0 otherwise. Through this model, we obtain the fitted probabilities of each subject being complete, denoted as π_i.

The DOOR probability can then be calculated using DOOR at Day 8 as the outcome following the algorithm below:

1. Name DOOR from the group that received placebo "sample 1" and the DOOR score ranks from the group that received IV bacteriophage "sample 2". Rename weights from sample 1 as w_{1i} and weights from sample 2 as w_{2i}.
2. Take the first observation in sample 2. If an observation in sample 2 has a smaller DOOR score rank than an observation in sample 1, then that observation in sample 2 gets an indicator of value of 1. Otherwise, if the observation in sample 2 is equal to the observation in sample 1, the observation in sample 2 gets an indicator value of ½.
3. Let π_{1i} be the fitted probability of being complete for each observation in sample 1 and π_{2i} be the fitted probability for being complete for each observation in sample 2 obtained from the logistic regression model with an indicator for having non-missing DOOR score rank as the outcome.
4. For each pair in step 2, create the weight w_j as the inverse of the probability of both values in the pair being non-missing, i.e., $w_j = 1/(\pi_{1i} \times \pi_{2i})$ with j being the index for observations in sample 2
5. For each pair in step 2, create the weighted indicator value as $w\_ind_j = w_j \times indicator_j$
6. Repeat step 2 through 5 for all observations in sample 2.
7. The DOOR probability can then be obtained by *DOOR_prob_IPW* = weighted average of all the indicator values in step 5, i.e.; $DOOR\_prob\_IPW = \frac{\sum_j w\_ind_j}{\sum w_j}$,

The DOOR probability (i.e., Pr(more desirable DOOR in IV bacteriophage) + 0.5 Pr(Equal DOOR)) using IPW is given by the value in *DOOR_prob_IPW.*

To estimate the 95% CIs for the DOOR probability, the approach discussed in Halperin et al. [2] after incorporating IPW weights is utilized. The superiority of IV bacteriophage vs placebo is concluded if the lower bound of the 95% CI for the DOOR probability is larger than 50%.

IPW will be used to handle missing data for the primary analysis of the DOOR endpoint. Percentage of subjects with missing DOOR data will be presented by time point and treatment group in Table 25.

A tipping point analysis will be performed to estimate the impact of missing data on the primary analysis of the DOOR (Table 27).

Pseudocode for Missingness model to estimate fitted probabilities and IPW weights:

Define complete as 1 for complete and 0 for missing and trt=1 for Placebo and 2 for IV bacteriophage.

```
proc logistic data = dat;
  model complete (event='1') = [trt];
  output out = out1 p = probs xbeta = logit;
run;
proc transpose data=out1 out=out2; by patid id trt; var probs; run;
data out2;
      set out2;
      wts=1/(probs_IVB * probs_pbo);
run;
```

8.2. Exploratory Analyses

8.2.1. Change in Lung Function Through Day 30 ± 7

Lung function will be measured using FEV1 from spirometry measurements collected at Days 1(Baseline), 2, 5, and 30.

The absolute change in lung function measured by FEV1 will be summarized by number of subjects, mean, SD, median, quartiles, minimum, and maximum in Table 34. The percent change in predicted FEV1 from baseline to Days 2, 5, and 30 will be presented by treatment group in Table 35. Predicted FEV1 will be calculated using the Global Lung Function Initiative (GLI) global standards. The baseline and post-baseline measures will be log-transformed before calculation of the percent change, then back-transformed before calculating the mean.

8.2.2. Characterization of Geographically Diverse *P. aeruginosa* Isolates Susceptibility to Bacteriophages

The changes in $\log_{10}$ *P. aeruginosa* colony counts through Day 30 ± 7 will be summarized by morphology and treatment group in Table 36. Changes will be summarized by number of subjects, mean, SD, median, quartiles, minimum, and maximum.

The proportion of *P. aeruginosa* isolates susceptible to each dose of bacteriophage will be presented by dose in Table 37. The 95% CI for the proportion of susceptible isolates in each treatment group will be calculated using the Wilson method and the 95% CI for the difference between IV bacteriophage and placebo will be calculated using the Miettinen–Nurminen method. Susceptibility testing results will be presented in Listing 13. Phage quantitiave polymerase chain reaction (qPCR) results will be presented in Listing 14.

8.2.3. Quality of Life Analysis

The CFQ-R will be administered at Baseline and Day 30 ± 7 (two timepoints) for Stage 2 subjects. Change at the Day 30 follow-up visit from baseline in CFQ-R will be presented by domain and treatment group in Table 38. For the definition of baseline, refer to Section 3.3.2. The CFQ-R results will be presented in Listing 15. This questionnaire contains a series of questions regarding several physical health and ability domains that subjects will answer as ‘Very True’, ‘Mostly True’, ‘Somewhat True’, or ‘Not at all True’ or alternatively ‘Always’, ‘Often’, ‘Sometimes’ or ‘Never’. Each question will receive a score of 1-4 with higher scores indicating more favorable QoL outcomes. Scores will be assigned to each domain based on the sum of the question scores. The analysis for this endpoint will be the change in the overall CFQ-R score from baseline at Day 30.

The CFRSD will be collected at all visits for Stage 2 subjects. Change from baseline through the Day 30 follow-up visit in CFRSD score will be presented by treatment group in Table 39. CFRSD results will be presented in Listing 16. The questions on the CFRSD will be scored in a similar way to those on the CFQ-R, however there will be no domain scores, only a single aggregate score for this QoL measurement. The analysis for this endpoint will be the change in the aggregate score from the Baseline visit to the highest score achieved on Days 2 through 30.

8.2.4. Subgroup Analyses

A subgroup analysis of the primary endpoints will be conducted to explore whether estimated treatment effects vary significantly between subcategories of trial subjects, including bacteriophage susceptibility and presence of co-infection with other organisms recovered on sputum cultures. Analysis of the difference in

mean change between IV bacteriophage and placebo arms and the $\log_{10}$-transformed difference in mean change, along with the corresponding 95% CIs, will be presented by subgroup in Table 22. A forest plot of the differences in *P. aeruginosa* colony counts is presented by subgroup in Figure 8 and a forest plot of differences in the $\log_{10}$ *P. aeruginosa* colony counts is presented by subgroup in Figure 9. Analysis of the primary DOOR endpoint at Day 8 will be presented by subgroup in Table 29 and a contingency table of DOOR by subgroup, treatment group, and time point will be presented in Table 30. A forest plot of DOOR probability in subgroups will be presented in Figure 11.

8.3. Interim Analyses

The interim microbiologic activity review will consist of a quantitative evaluation of potential effect sizes and associated precision using a predicted intervals and PIPs approach. Predicted intervals for DOOR probability through Day 8 + 3 will be calculated under the following range of assumptions:

1. The trends in outcomes observed at the time of the interim analysis continue to the end of study.
2. Both DOOR distributions are identical. Null distribution of cell proportions for the DOOR of IV bacteriophage dose vs placebo, will be calculated as $\bar{P}_i = rP_{1i} + (1-r)P_{2i}$ $(i = 1, \ldots D)$, where
   - r is the proportion of IV bacteriophage subjects
   - P_1 is the proportion of subjects in the IV bacteriophage dose group in the ith DOOR category
   - P_2 is the proportion of subjects in the placebo group in the ith DOOR category
   - D is the number of DOOR categories
3. Best and worst-case scenarios for remaining outcomes. The best-case scenario will be assumed as DOOR = 1 for all remaining subjects in the bacteriophage group and observed placebo proportions at the time of the interim analysis for all remaining subjects in the placebo group. Worst case scenario will be assumed as DOOR = 4 for all remaining subjects in the bacteriophage group and observed placebo proportions at the time of the interim analysis for all remaining subjects in the placebo group.

These PIPs provide a prediction of the trial results were the trial to continue as planned under the above assumptions regarding future data [3]. For each assumption, 10,000 complete datasets (with N = 20 subjects in each treatment group for current sample size or N = 25 for increased sample size) will be simulated and used to calculate the probability of rejecting the null hypothesis for each scenario.

Similar to DOOR, changes in $\log_{10}$ *P. aeruginosa* colony counts (total and each morphology) in sputum cultures from administration of IV bacteriophages through Day 8 + 3, will be evaluated, using PIPs to assess the precision for measuring differences in $\log_{10}$ CFU/mL count. Predicted intervals will be calculated under a range of assumptions including:

1. The trends in outcomes observed at the time of the interim analysis continue to the end of study
2. Best case: remaining bacteriophage subjects simulated to have > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL, remaining placebo subjects simulated to have the same trend observed in placebo subjects at the time of the interim analysis
3. Worst case: remaining bacteriophage subjects simulated to have < 1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL, remaining placebo subjects simulated to have the same trend observed in placebo subjects at the time of the interim analysis

The planned total Stage 2a + Stage 2b sample size (20 subjects per treatment group) will be reevaluated after the completion of Stage 2a. If necessary, the final sample size will be increased to up to 25 subjects for the placebo arm and up to 25 subjects for the selected bacteriophage dose to provide the desired precision of estimates.

Tables, listings, and figures for the planned interim analyses will not be shown in this SAP. They will instead appear in the Phage Advisory Group Charter document.

9. SAFETY EVALUATION

All safety analyses will be presented using the Safety Population unless otherwise noted.

When calculating the incidence of AEs and SAEs (i.e., on a per subject basis), each subject will be counted once for their most related and/or highest severity AE reported, and any repetitions within a subject will be ignored for events coded in the same category by MedDRA. The denominators for percent values will be indicated within the table or table header and denominators will consist of the maximal size of the Safety Population in the indicated observation period.

9.1. Demographic and Other Baseline Characteristics

Categorical demographic variables, such as sex, ethnicity, and race, will be summarized by treatment group for the ITT population in Table 14 and for the Safety Population in Table 15. Ethnicity will be categorized "Hispanic or Latino," or "Not Hispanic or Latino," "Unknown," or "Not Reported." In accordance with National Institutes of Health (NIH) reporting policies, subjects may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the CRF as "No" to each race option. Continuous baseline variables, such as age, height, and weight, will be summarized by treatment group for the ITT population in Table 16 and for the Safety Population in Table 17. Individual subject listings will be presented for all demographic and baseline characteristics in Listing 6.

9.1.1. Prior and Concurrent Medical Conditions

All current illnesses and past pre-existing medical conditions will be MedDRA coded using the MedDRA dictionary version 25.0 or higher.

Number and percentage of subjects' pre-existing medical conditions will be presented by the MedDRA SOC and treatment group for the ITT population in Table 18.

Individual subject listings will be presented for all pre-existing and concurrent medical conditions in Listing 7.

9.1.2. Prior and Concomitant Medications

Prior medication is defined as any medication taken before the first date of study product or placebo administration. Concomitant medication is defined as any medication started on or after the first date of study product or placebo administration.

Summaries of medications that were started prior to dosing and continuing at the time of dosing will be coded to the Anatomical Therapeutic Classification (ATC) using the World Health Organization (WHO) Drug Dictionary. The use of prior medications will be summarized in Table 123, Table 124, and Table 125 and concomitant medications will be summarized in Table 126, Table 127, and Table 128, by the number and proportion of subjects in each arm and treatment group within each ATC1 and ATC2 code for the Safety Population. If a subject took a specific medication multiple times or took multiple medications within a specific therapeutic class, that subject would be counted only once for the coded drug name or therapeutic class.

A by-subject listing of prior and concomitant medication use will be presented in Listing 25 and Listing 26, respectively.

9.2. Measurements of Treatment Compliance

Dates of first treatment will be summarized by site and treatment group in Table 9. Treatment administration information will be included in Listing 8. A listing of infusion interruptions will be presented in Listing 9. A listing of all subjects who took at least one dose of study product is provided in Listing 1.

9.3. Adverse Events

When calculating the proportions of subjects with AEs within a given MedDRA category, subjects will be counted once for each dosing period within the same MedDRA category, and the event will be reported according to the highest severity recorded throughout the indicated time period (separately for related and unrelated AEs when both severity and relatedness are tabulated). Repeated AEs will be ignored. When calculating the number of AEs that occurred, all AEs will be summarized by treatment group, including repetitions. All reported AEs will be included in the summaries and analyses.

9.3.1. Treatment-Emergent Adverse Events of Grade 2 or Higher

The primary safety endpoint for this study is the number of Grade 2 or higher TEAEs through Day 30 ± 7. This endpoint will be analyzed using the ITT population and is described further in Section 8.1.1.

9.3.2. Unsolicited Adverse Events

The proportion of subjects reporting at least one unsolicited AE will be summarized by MedDRA SOC, HLT, and PT and by treatment group. Denominators for proportions are the number of subjects in the Safety Population in each treatment group.

Unsolicited AEs by subject will be presented in Listing 17.

The following summaries for unsolicited AEs will be presented:

- Overall summary of AEs (Table 40).
- AEs occurring in 5% of subjects in any treatment group are summarized by MedDRA SOC, HLT, and PT and by treatment group in Stage 1 (Table 41), Stage 2a (Table 42), and Stage 2a and 2b (Table 43).
- Subject incidence and total frequency of unsolicited AEs by MedDRA SOC, HLT, and PT and by treatment group with 95% CI, calculated using an exact Clopper-Pearson confidence interval in Stage 1 (Table 46), Stage 2a (Table 47), and Stage 2a and 2b (Table 48).
- Summary of unsolicited AEs by severity, relationship to study product, MedDRA SOC, HLT, and PT and by treatment group in Stage 1 (Table 49), Stage 2a (Table 50), and Stage 2a and 2b (Table 51).
- Summary of TEAEs, on-therapy SAEs, and AEs leading to discontinuation by MedDRA PT in Stage 1 (Table 52), Stage 2a (Table 53), and Stage 2a and 2b (Table 54). TEAEs are any AEs that were not present before the first dose of study product or were present before the first dose of study product and increased in severity during the treatment period. On-therapy SAEs are any SAEs occurring during or after the infusion of bacteriophage/placebo product.
- Summary of fatal on-therapy SAEs by MedDRA PT and treatment group (Table 55).
- Bar chart frequency of AEs by severity, MedDRA SOC, and treatment group in Stage 1 (Figure 14), Stage 2a (Figure 15), and Stage 2a and 2b (Figure 16).
- Bar chart incidence of AEs by severity, MedDRA SOC, and treatment group in Stage 1 (Figure 17), Stage 2a (Figure 18), and Stage 2a and 2b (Figure 19).

9.3.3. Events of Special Interest (ESIs)

The following events of special interest (ESIs) will be collected from the time of first administration of study product until Visit 5, Day 8 + 3 day:

- Pulmonary exacerbation, defined as:
  - Initiation of oral or IV antibiotics by the treating clinicians for respiratory symptoms,

  OR
  - Four or more of the following signs/symptoms:
    - Increase in both sputum quality and production
    - New or increased hemoptysis
    - Worsening cough
    - Increased shortness of breath
    - New onset malaise/fatigue/lethargy
    - Temperature > 38°C
    - Change in physical examination of the chest
    - Decrease in FEV1 > 10% from Baseline; and/or
    - Radiographic changes consistent with a pulmonary exacerbation.

Any ESI that meets the criteria of an SAE will be recorded and reported as an SAE instead of an ESI.

9.4. Deaths, Serious Adverse Events and Other Significant Adverse Events

Individual data listings of SAEs, ESIs, AEs leading to study product discontinuation, and deaths will be provided in Table 56, Table 57, Table 58, and Table 59, respectively.

Listings will include Subject ID, event description, date of onset, assessment of severity, relationship to study product and alternate etiology, date of resolution, seriousness, and outcome.

9.5. Pregnancies

Individual data listings of pregnancy reports will be provided if a pregnancy occurs post dosing:

- Maternal information will be presented in Listing 27.
- Gravida and para information will be presented in Listing 28.
- Live birth outcomes will be presented in Listing 29, and still birth outcomes will be presented in Listing 30.
- Spontaneous, elective, or therapeutic abortion outcomes will be presented in Listing 31.

9.6. Clinical Laboratory Evaluations

After Protocol v5.0, Visit 6 (Study Day 12 + 7) was removed from the visit schedule for any subjects enrolling in Stage 2a or Stage 2b. Any laboratory summaries for Day 12 data will only show data from Stage 1 subjects. Any laboratory data collected during this visit for Stage 2a subjects who enrolled under the previous version of the Protocol will be included in lab listings only.

The distribution of laboratory results will be presented by severity, time point, and treatment group. Clinical chemistry parameters will be displayed beginning with Table 63 and continuing through Table 71, hematology parameters will be displayed beginning with Table 80 and continuing through Table 88, and liver function tests parameters will be displayed beginning with Table 97 and continuing through Table 104. Descriptive statistics, including mean, SD, median, minimum, maximum, and change from baseline by time point and treatment group will be presented beginning with Table 72 and continuing through Table 79 for clinical chemistry parameters, beginning with Table 89 and continuing through Table 96 for hematology parameters, and beginning with Table 105 and continuing through Table 111 for liver function test parameters.

Graphical presentations of change from baseline at scheduled visits by treatment group and time point for each parameter as a series of box plots. Chemistry parameters will be presented beginning with Figure 20 and continuing through Figure 27. Hematology parameters will be presented beginning with Figure 28 and continuing through Figure 35. Liver function parameters will be presented beginning with Figure 36 and continuing through Figure 42.

Abnormal chemistry results will be presented in Table 60, abnormal hematology results will be presented in Table 61, and abnormal liver function results will be presented in Table 62.

All chemistry results will be presented in Listing 18, all hematology results will be presented in Listing 19 and all liver function results will be presented in Listing 20.

9.7. Vital Signs and Physical Evaluations

Descriptive statistics and change from baseline will be summarized for the following vital signs: systolic and diastolic blood pressure (BP) in millimeters of mercury (mmHg), heart rate (beats per minute [BPM]), respiratory rate, and body temperature in degrees Celsius (°C; oral measurement). Vital signs will be collected at baseline, Days 2, 5, 12, 30, and ET or unscheduled study visits.

The proportion of subjects with mild, moderate, or severe vital sign results will be presented by parameter, treatment group, and time point beginning with Table 112 and continuing through Table 117. Vital sign measurement values and change from baseline will be presented by parameter, treatment group, and time point beginning with Table 118 and continuing through Table 122. All vital sign results will be presented in Listing 21. Graphical presentation of change from baseline at scheduled visits by treatment group and time point will be presented for each vital sign parameter beginning with Figure 43 and continuing through Figure 47.

Symptom directed physical examinations will be performed at baseline, Days 2, 5, 12, 30, and ET or unscheduled study visits. A listing of physical exam findings will be presented in Listing 22. A listing of review of systems findings will be presented in Listing 23.

Spirometry will occur prior to required sputum collections. Spirometry values will be presented in Listing 24.

10. PHARMACOKINETICS

Analysis of PK endpoints will be provided in separate analysis plan document.

11. IMMUNOGENICITY

Not applicable.

12. OTHER ANALYSES

Not applicable.

13. REPORTING CONVENTIONS

P-values ≥ 0.001 and ≤ 0.999 will be reported to 3 decimal places; p-values less than 0.001 will be reported as "< 0.001." The mean, standard deviation, and other statistics will be reported to 1 decimal place greater than the original data. The minimum and maximum will use the same number of decimal places as the original data. Proportions will be reported to the nearest hundredth; values greater than zero but < 0.01 will be presented as "< 0.01". Percentages will be reported to the nearest whole number; values greater than zero but < 1% will be presented as "< 1%"; values greater than 99% but less than 100% will be reported as "> 99%". Estimated parameters, not on the same scale as raw observations (e.g., regression coefficients) will be reported to 3 significant figures.

14. TECHNICAL DETAILS

SAS version 9.4 or above and R versions 3.2 or above will be used to generate the tables, figures, and listings.

15. SUMMARY OF CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

No changes have occurred in the conduct of the study or planned analyses.

16. REFERENCES

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17. LISTING OF TABLES, FIGURES, AND LISTINGS

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9.5.1 Microbiological Activity/Benefit to Risk Profile and Safety Measurements Assessed and Flow Chart

Table 1: Schedule of Study Procedures

Visit	Screening	Baseline/Dosing	Follow-up Visits					Early Termination Visit[1]/ Unscheduled Study Visit
Visit Number	**1**	**2**	**3**	**4**	**5[18]**	**6[19]**	**7**	**N/A**
Day (Window)	**Up to Day -7**	**1**	**2**	**5 ± 2**	**8 + 3**	**12 + 7**	**30 ± 7**	**Variable**
Informed Consent	X							
Eligibility Criteria	X	X						
Serum HCG Pregnancy Test	X[2]							
Urine Pregnancy Test		X[2]						
Demographics	X							
Height and Weight Measurement	X							
Medical History[3]	X							
Medication History[4]	X							
Review of systems	X	X	X	X	X	X	X	X
Treatment Assignment (**Stage 1**) /Randomization (**Stage 2**)		X						
Administration of Study Product		X						
Concomitant Medications		X	X	X	X	X	X	X
Physical Examination	X[5]							
Symptom Directed Physical Examination		X[6]	X	X		X	X	X
Vital Signs	X[5]	X[6]	X	X		X	X	X
Spirometry	X	X[7]	X	X		X	X	X[8]
Sputum Collection[9]	X	X[10]	X	X	X	X	X	X
Clinical Chemistry		X[11,15]	X	X		X	X	X[12]
Liver Function Tests	X[13]	X[11,15]	X	X		X	X	X[12]
Hematology		X[11,15]	X	X		X	X	X[12]
Serum for PK		X[14]	X					
CFQ-R (**Stage 2 only**)[17]		X[15]					X	

Table 1: Schedule of Study Procedures *(continued)*

Visit	Screening	Baseline/Dosing	Follow-up Visits					Early Termination Visit[1]/ Unscheduled Study Visit
Visit Number	**1**	**2**	**3**	**4**	**5[18]**	**6[19]**	**7**	**N/A**
Day (Window)	**Up to Day -7**	**1**	**2**	**5 ± 2**	**8 + 3**	**12 + 7**	**30 ± 7**	**Variable**
CFRSD (**Stage 2 only**)[17]		X[15]	X	X	X		X	X
Safety Assessment		X	X	X	X	X	X	X
Events of Special Interest		X	X	X	X			X[16]

Abbreviations: CFQ-R: Cystic fibrosis questionnaire-revised; CFRSD: Cystic fibrosis respiratory symptom diary; HCG: Human chorionic gonadotropin; N/A: Not Applicable; PK: Pharmacokinetic

[1]May be conducted by telephone call if subject is too ill to attend in-person or virtual visit, per local investigator.

[2]Pregnancy testing will be performed for all female subjects of childbearing potential and the results of both the HCG test at screening and urine test at baseline must be negative prior to treatment assignment/randomization.

[3]Including full account of the subject's routine respiratory physiotherapy regimen.

[4]Medication history within the past 30 days and those that remain active.

[5]Standard of care results obtained for clinical care purposes within 72 hours of screening are acceptable for screening.

[6]Before administration of study product or placebo AND 30-60 minutes after completed administration of study product or placebo.

[7]Spirometry to occur prior to study product/placebo administration and within 30 minutes to 2 hours after study product/placebo administration.

[8]If the visit occurs > 7 days after a scheduled visit. If the visit occurs ≤ 7 days after a scheduled visit, spirometry may be performed at the discretion of the local investigator.

[9]At in-person visits. To be completed after spirometry, as considered necessary by the local investigator to increase sputum production.

[10]Sputum will be obtained pre-infusion and post-infusion for microbiological and PK assessments (refer to the protocol, Sections 7.2.1 and 7.2.2 for details).

[11]Standard of care labs obtained within 7 days of Baseline may be used to record these results, otherwise, assessments must be done as a study procedure.

[12]If the visit occurs > 7 days after a scheduled visit. If the visit occurs ≤ 7 days after a scheduled visit, laboratory tests may be collected at the discretion of the local investigator.

[13]AST, ALT, and total bilirubin only.

[14]Serum will be obtained pre-infusion and post-infusion for PK assessments (refer to the protocol, Section 7.2.2 for details).

[15]Prior to administration of Study Product/Placebo.

[16]If the visit occurs prior to Visit 5, Day 8 + 3.

[17]Preferably before the collection of study data. If subject is ready to produce sputum, prioritize sputum collection over administration of the CFQ-R/CFRSD.

[18]In Stage 2, this is a virtual visit.

[19]This visit is only applicable for Stage 1.

10.2 Protocol Deviations

Table 2: Distribution of Protocol Deviations by Category, Type, and Treatment Group, Stage 1 – ITT Population

Category	Deviation Type	$4x10^7$ PFU Dose (N=X)		$4x10^8$ PFU Dose (N=X)		$4x10^9$ PFU Dose (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
Eligibility/enrollment	Any type								
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x
	Met exclusion criterion								
	ICF not signed prior to study procedures								
	Other								
Treatment administration schedule	Any type								
	Out of window visit								
	Missed visit/visit not conducted								
	Missed treatment administration								
	Delayed treatment administration								
	Other								
Follow-up visit schedule	Any type								
	Out of window visit								
	Missed visit/visit not conducted								
	Other								

Table 2: Distribution of Protocol Deviations by Category, Type, and Treatment Group *(continued)*

Category	Deviation Type	$4x10^7$ PFU Dose (N=X)		$4x10^8$ PFU Dose (N=X)		$4x10^9$ PFU Dose (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
Protocol procedure/assessment	Any type								
	Incorrect version of ICF signed								
	Blood not collected								
	Urine not collected								
	Sputum not collected								
	Other specimen not collected								
	Too few aliquots obtained								
	Specimen result not obtained								
	Required procedure not conducted								
	Required procedure done incorrectly								
	Study product temperature excursion								
	Specimen temperature excursion								
	Other								
Treatment administration	Any type								
	Required procedure done incorrectly								
	Required procedure not conducted within window								
	Study product temperature excursion								
	Other								
Blinding policy/procedure	Any type								
	Treatment unblinded								
	Other								

Tables with similar format [Implementation note: these tables will contain a 'Placebo' column to the right of the $4x10^9$ PFU column]:

Table 3: Distribution of Protocol Deviations by Category, Type, and Treatment Group, Stage 2a – ITT Population

Table 4: Distribution of Protocol Deviations by Category, Type, and Treatment Group, Stage 2a and 2b – ITT Population

14.1 Description of Study Subjects

14.1.1 Disposition of Subjects

Table 5: Subject Disposition by Treatment Group – ITT Population

Subject Disposition	$4x10^7$ PFU Dose (N=X)		$4x10^8$ PFU Dose (N=X)		$4x10^9$ PFU Dose (N=X)		Placebo (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	n	%
Stage 1										
Screened	--	--	--	--	--	--	--	--	x	--
Enrolled/Randomized	x	100	x	100	x	100	--	--	x	100
Received Treatment	x	xx	x	xx	x	xx	--	--	x	xx
Early Termination	x	xx	x	xx	x	xx	--	--	x	xx
Completed Visit 3 (Study Day 2)	x	xx	x	xx	x	xx	--	--	x	xx
Completed Visit 4 (Study Day 5 ± 2)	x	xx	x	xx	x	xx	--	--	x	xx
Completed Visit 5 (Study Day 8 + 3)	x	xx	x	xx	x	xx	--	--	x	xx
Completed Visit 6 (Study Day 12 + 7)	x	xx	x	xx	x	xx	--	--	x	xx
Completed Visit 7 (Study Day 30 ± 7)	x	xx	x	xx	x	xx	--	--	x	xx
Completed All Follow-up Visits	x	xx	x	xx	x	xx	--	--	x	xx
Stage 2a										
…	x	xx	x	xx	x	xx	x	xx	x	xx
Stage 2a and 2b										
…	x	xx	x	xx	x	xx	x	xx	x	xx

Note: N=Number of subjects in the ITT population.

Table 6: Subject Disposition by Treatment Group – Safety Population

This table will repeat Table 3 limited to the Safety Population.

Table 7: Subject Disposition by Site – Screened Population

Subject Disposition	n	%
Site 1 (N=X)		
Enrolled/Randomized	x	100
Received Treatment	x	xx
Early Termination	x	xx
Completed Visit 3 (Study Day 2)	x	xx
Completed Visit 4 (Study Day 5 ± 2)	x	xx
Completed Visit 5 (Study Day 8 + 3)	x	xx
Completed Visit 6 (Study Day 12 + 7)	x	xx
Completed Visit 7 (Study Day 30 ± 7)	x	xx
Completed All Follow-up Visits	x	xx
Site 2 (N=X)		
…		
All Sites (N=X)		
Screened	x	--
Enrolled/Randomized	x	100
Received Treatment	x	xx
Early Termination	x	xx
Completed Visit 3 (Study Day 2)	x	xx
Completed Visit 4 (Study Day 5 ± 2)	x	xx
Completed Visit 5 (Study Day 8 + 3)	x	xx
Completed Visit 6 (Study Day 12 + 7)	x	xx
Completed Visit 7 (Study Day 30 ± 7)	x	xx
Completed All Follow-up Visits	x	xx

Note: N=Number of subjects in the ITT population.

Table 8: Analysis Populations by Treatment Group

Analysis Populations	Reason Subjects Excluded	$4x10^7$ PFU Dose (N=X)		$4x10^8$ PFU Dose (N=X)		$4x10^9$ PFU Dose (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%
Stage 1											
ITT	Any Reason	x	xx	x	xx	x	xx	-	-	x	xx
	Subject not randomized	x	xx	x	xx	x	xx	-	-	x	xx
Safety	Any Reason	x	xx	x	xx	x	xx	-	-	x	xx
	Subject not treated with at least one dose of study product	x	xx	x	xx	x	xx	-	-	x	xx
Pharmacokinetics	Any Reason	x	xx	x	xx	x	xx	-	-	x	xx
	Subject received placebo	x	xx	x	xx	x	xx	-	-	x	xx
	Assigned dose not received or completed	x	xx	x	xx	x	xx	-	-	x	xx
	Did not contribute at least two sputum samples	x	xx	x	xx	x	xx	-	-	x	xx
	Did not contribute at least two blood samples	x	xx	x	xx	x	xx	-	-	x	xx
Stage 2a											
…		x	xx	x	xx	x	xx	x	xx	x	xx
Stage 2a and 2b											
…		x	xx	x	xx	x	xx	x	xx	x	xx

Note: N=Number of subjects in the ITT population.

Table 9: Dates of First Treatment by Site and Treatment Group – ITT Population

[Implementation note: Replace site numbers by site names and sort the site list alphabetically. All subjects receiving IV bacteriophage will be shown as pooled together in this table.]

Site	Treatment Group	MMMYYYY-MMMYYYY	MMMYYYY-MMMYYYY
Any	Any	x	x
Any Site	IV Bacteriophage	x	x
	Placebo	x	x
Site 1	IV Bacteriophage	x	x
	Placebo	x	x
Site 2	IV Bacteriophage	x	x
	Placebo	x	x
Site 3	IV Bacteriophage	x	x
	Placebo	x	x
Site 4	IV Bacteriophage	x	x
	Placebo	x	x
Site 5	IV Bacteriophage	x	x
	Placebo	x	x
Site 6	IV Bacteriophage	x	x
	Placebo	x	x
[Repeat for all sites that enrolled at least one subject.]			

Table 10: Ineligibility Summary of Screen Failures, Stage 1

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Total Number of Screen Failures (N=X)			
Inclusion and Exclusion	Number of subjects failing any eligibility criterion	x	100
Inclusion	Any inclusion criterion	x	xx
	Adult (≥ 18 years) at the time of screening	x	xx
	Confirmed CF diagnosis based on a compatible clinical syndrome confirmed by either an abnormal sweat chloride testing or CFTR gene variations	x	xx
	Likely able to produce at least 2 mL of sputum during a 30-minute sputum collection following a hypertonic saline treatment or other approach to increase sputum production	x	xx
	P. aeruginosa (regardless of CFU/mL) isolated from a sputum, throat culture, or other respiratory specimen in the past 12 months	x	xx
	Confirmed *P. aeruginosa* isolation from a sample of expectorated sputum at the Screening Visit	x	xx
	Capable of providing informed consent	x	xx
	Capable and willing to complete all study visits and perform all procedures required by this protocol	x	xx
Exclusion	Any exclusion criterion	x	xx
	Body weight < 30 kg	x	xx
	FEV1 < 20% of predicted value at screening, using the Hankinson equations	x	xx
	Elevated LFTs obtained at screening	x	xx
	Acute clinical illness requiring a new oral, parenteral, or inhaled antibiotic(s) ≤ 30 days prior to the Baseline Visit	x	xx
	Women who are pregnant, planning to become pregnant during the study period, or breastfeeding	x	xx
	Active treatment of any mycobacteria or fungal organisms ≤ 30 days prior to baseline. Chronic treatment for suppression of fungal populations is allowable	x	xx
	Anticipated need to change chronic antibiotic regimens during the study period	x	xx
	Known allergy to any component of the study product	x	xx
	Any significant finding that, in the opinion of the investigator, would make it unsafe for the subject to participate in this study	x	xx
	Enrolled in a clinical trial within ≤ 30 days of the Baseline/Dosing Visit, or participating in a clinical trial while enrolled in this clinical trial (inclusive of vaccine trials)	x	xx
	Currently or previously enrolled in this study	x	xx
Eligible but not Enrolled	Any Reason	x	xx
	[Reason 1]	x	xx
	[Reason 2]	x	xx

a More than one criterion may be marked per subject.
b Denominator for percentages is the total number of screen failures.

Tables with similar format:

Table 11: Ineligibility Summary of Screen Failures, Stage 2a

Table 12: Ineligibility Summary of Screen Failures, Stage 2a and 2b

Table 13: Reasons for Early Termination – Safety Population

Reason for Early Termination	$4x10^7$ PFU Dose (N=X)		$4x10^8$ PFU Dose (N=X)		$4x10^9$ PFU Dose (N=X)		Placebo (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	%	n
Stage 1										
Any Reason	x	xx	x	xx	x	xx	-	-	x	xx
Serious adverse event (other than death)	x	xx	x	xx	x	xx	-	-	x	xx
Adverse event, other than serious adverse event	x	xx	x	xx	x	xx	-	-	x	xx
Event of special interest	x	xx	x	xx	x	xx	-	-	x	xx
Lost to follow-up	x	xx	x	xx	x	xx	-	-	x	xx
Protocol deviation	x	xx	x	xx	x	xx	-	-	x	xx
Voluntary withdrawal by subject	x	xx	x	xx	x	xx	-	-	x	xx
Withdrawal by investigator	x	xx	x	xx	x	xx	-	-	x	xx
COVID-19 pandemic	x	xx	x	xx	x	xx	-	-	x	xx
Termination of site by sponsor	x	xx	x	xx	x	xx	-	-	x	xx
Termination of study by sponsor	x	xx	x	xx	x	xx	-	-	x	xx
Death	x	xx	x	xx	x	xx	-	-	x	xx
Enrolled but treatment not administered	x	xx	x	xx	x	xx	-	-	x	xx
Not eligible at enrollment	x	xx	x	xx	x	xx	-	-	x	xx
Became ineligible after enrollment	x	xx	x	xx	x	xx	-	-	x	xx
Other	x	xx	x	xx	x	xx	-	-	x	xx
Stage 2a										
…	x	xx	x	xx	x	xx	x	xx	x	xx
Stage 2a and 2b										
…	x	xx	x	xx	x	xx	x	xx	x	xx

Note: N=Number of subjects in the Safety Population.

14.1.2 Demographic Data by Study Group

Table 14: Summary of Categorical Demographic and Baseline Characteristics by Treatment Group – ITT Population

Variable	Characteristic	$4x10^7$ PFU Dose (N=X)		$4x10^8$ PFU Dose (N=X)		$4x10^9$ PFU Dose (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%
Stage 1											
Sex	Male	x	xx	x	xx	x	xx	-	-	x	xx
	Female	x	xx	x	xx	x	xx	-	-	x	xx
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	-	-	x	xx
	Hispanic or Latino	x	xx	x	xx	x	xx	-	-	x	xx
	Not Reported	x	xx	x	xx	x	xx	-	-	x	xx
	Unknown	x	xx	x	xx	x	xx	-	-	x	xx
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	-	-	x	xx
	Asian	x	xx	x	xx	x	xx	-	-	x	xx
	Native Hawaiian or Other Pacific Islander	x	xx	x	xx	x	xx	-	-	x	xx
	Black or African American	x	xx	x	xx	x	xx	-	-	x	xx
	White	x	xx	x	xx	x	xx	-	-	x	xx
	Multi-Racial	x	xx	x	xx	x	xx	-	-	x	xx
	Unknown	x	xx	x	xx	x	xx	-	-	x	xx
Stage 2a											
…		x	xx	x	xx	x	xx	x	xx	x	xx
Stage 2a and 2b											
…		x	xx	x	xx	x	xx	x	xx	x	xx

Note: N=Number of subjects in the ITT population.

Table 15: Summary of Categorical Demographic and Baseline Characteristics by Treatment Group – Safety Population

This table will repeat Table 10 limited to the Safety Population.

Table 16: Summary of Continuous Demographic and Baseline Characteristics by Treatment Group – ITT Population

Variable	Statistic	$4x10^7$ PFU Dose (N=X)	$4x10^8$ PFU Dose (N=X)	$4x10^9$ PFU Dose (N=X)	Placebo (N=X)	All Subjects (N=X)
Stage 1						
Age (years)	Mean	Xx	xx	xx	-	xx
	Standard Deviation	Xx	xx	xx	-	xx
	Median	Xx	xx	xx	-	xx
	Minimum	X	x	x	-	x
	Maximum	X	x	x	-	x
Height (cm)	Mean	Xx	xx	xx	-	xx
	Standard Deviation	Xx	xx	xx	-	xx
	Median	Xx	xx	xx	-	xx
	Minimum	X	x	x	-	x
	Maximum	X	x	x	-	x
Weight (kg)	Mean	Xx	xx	xx	-	xx
	Standard Deviation	Xx	xx	xx	-	xx
	Median	Xx	xx	xx	-	xx
	Minimum	X	x	x	-	x
	Maximum	X	x	x	-	x
BMI (kg/m^2)	Mean	Xx	xx	xx	-	xx
	Standard Deviation	Xx	xx	xx	-	xx
	Median	Xx	xx	xx	-	xx
	Minimum	X	x	X	-	x
	Maximum	X	x	X	-	x
Stage 2a						
…		Xx	xx	xx	xx	xx
Stage 2a and 2b						
…		Xx	xx	xx	xx	xx

Note: N=Number of subjects in the ITT population.

Table 17: Summary of Continuous Demographic and Baseline Characteristics by Treatment Group – Safety Population

This table will repeat Table 13 limited to the safety population.

14.1.3 Prior and Concurrent Medical Conditions

Table 18: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group – ITT Population

MedDRA System Organ Class	$4x10^7$ PFU Dose (N=X)		$4x10^8$ PFU Dose (N=X)		$4x10^9$ PFU Dose (N=X)		Placebo (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	n	%
Stage 1										
Any SOC	x	xx	x	xx	x	Xx	-	-	x	xx
[SOC 1]	x	xx	x	xx	x	Xx	-	-	x	xx
[SOC 2]	x	xx	x	xx	x	Xx	-	-	x	xx
…	x	xx	x	xx	x	Xx	-	-	x	xx
Stage 2a										
…	x	xx	x	xx	x	Xx	x	xx	x	xx
Stage 2a and 2b										
…	x	xx	x	xx	x	Xx	x	xx	x	xx

Note: N=Number of subjects in the ITT population.
n=Number of subjects reporting medical history within the specified SOC. A subject is only counted once per SOC.

14.2 Microbiological Activity and Benefit to Risk Profile Data

Table 19: Change from Baseline in *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures by Treatment Group – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	Treatment Group	Total Colony Counts						Change from Baseline						
		n	Mean	SD	Median	Q1, Q3[a]	Min, Max	n	Mean	SD	Median	Q1, Q3[a]	Min, Max	95% CI[b]
Baseline	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	-	-	-	-	-	-	-
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	-	-	-	-	-	-	-
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Maximum	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx

Notes: N=Number of subjects in the ITT Population in Stage 2a and 2b.
n=Number of subjects in the ITT Population with non-missing colony counts at the time point of interest. For the change from baseline, n represents the number of subjects in the ITT population with non-missing values at baseline and at the time point being assessed.
SD=Standard Deviation
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
[a]Q1 and Q3 represent the 25th and 75th percentiles, respectively
[b]95% CI (confidence interval) is calculated from a t-distribution.

Table 20: Change from Baseline in log_{10} *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures by Treatment Group – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected Dose' will be replaced with the dose chosen by the interim analysis].

Time Point	Treatment Group	log_{10} Total Colony Counts						Change from Baseline						
		n	Mean	SD	Median	Q1, Q3[a]	Min, Max	n	Mean	SD	Median	Q1, Q3[a]	Min, Max	95% CI[b]
Baseline	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	-	-	-	-	-	-	-
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	-	-	-	-	-	-	-
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Maximum	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx

Notes: N=Number of subjects in the ITT Population in Stage 2a and 2b.
n=Number of subjects in the ITT Population with non-missing colony counts at the time point of interest. For the change from baseline, n represents the number of subjects in the ITT population with non-missing values at baseline and at the time point being assessed.
SD=Standard Deviation
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
[a]Q1 and Q3 represent the 25th and 75th percentiles, respectively.
[b]95% CI (confidence interval) is calculated from a t-distribution.

Table 21: Difference in Mean Change from Baseline in *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures – ITT Population, Stage 2a and 2b

[Implementation note: The 95% CI for the difference in means is computed from Welch's t-test.]

Time Point	Difference in *P. aeruginosa* CFU/mL Mean Change from Baseline (95% CI[a])	Difference in $\log_{10}$ *P. aeruginosa* CFU/mL Mean Change from Baseline (95% CI[a])
Day 1 Post-infusion	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Day 2	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Day 5	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Day 8	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Day 30	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Maximum	xx (xx.x, xx.x)	xx (xx.x, xx.x)

Notes: Difference calculated as Placebo – IV Bacteriophage.
[a]The 95% CI for the difference in means is computed from Welch's t-test.

Table 22: Subgroup Analysis of Difference in Mean Change from Baseline in *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures – ITT Population, Stage 2a and 2b

[Implementation note: The following subgroups will be included in this analysis: Susceptible to bacteriophages – Yes, Susceptible to bacteriophages – Yes, Presence of Co-infection with Organism X – Yes, Presence of Co-infection with Organism X – No.

Implementation note: The 95% CI for the difference in means is computed from Welch's t-test.]

Subgroup	Time Point	n_b (%)	n_p (%)	Difference in Mean Change from Baseline (95% CI[a])	Difference log_{10} in Mean Change from Baseline (95% CI[a])
Susceptible to Bacteriophages – Yes	Day 1 Post-infusion	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Day 2	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Day 5	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Day 8	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Day 30	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Maximum	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
…					
Presence of Co-infection with Organism X – No	Day 1 Post-infusion	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)

Notes: Difference calculated as Placebo – IV Bacteriophage. N_b=number of subjects in the ITT population who received IV bacteriophage within the subgroup category. N_p=number of subjects in the ITT population who received placebo within the subgroup category. Denominator for percentages is the total number of IV bacteriophage subjects in the ITT population for n_b and the total number of placebo subjects in the ITT population for n_p.

[a] The 95% CI for the difference in means is computed from Welch's t-test.

Table 23: AUC of log_{10} *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures Over Time – ITT Population, Stage 2a and 2b

Time Point	Treatment Group	AUC				
		n	Mean	SD	Median	Min, Max
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Maximum	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x

Notes: N=Number of subjects in the ITT Population in Stage 2a and 2b.
n=Number of subjects in the ITT Population with non-missing colony counts at the time point of interest.
SD=Standard Deviation
AUC will be calculated using the linear trapezoidal rule as the area under the curve between baseline and the given time point.

Table 24: Difference in AUC of log_{10} *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis. The 95% CI for the difference in means is computed from Welch's t-test].

Time Point	Treatment Group	Difference in AUC	95% CI[a]
Day 1 Post-infusion	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Day 2	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Day 5	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Day 8	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Day 30	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Maximum	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x

Notes: AUC will be calculated using the linear trapezoidal rule as the area under the curve between baseline and the given time point.
[a] The 95% CI for the difference in means is computed from Welch's t-test.

Table 25: Percentage of Subjects with Missing DOOR Data by Time Point and Treatment Group - ITT Population, Stage 2a and 2b

[Implementation note: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.]

	Selected IV Bacteriophage Dose (N=X)		Placebo (N=X)		All Subjects (N=X)	
Time Point	**n**	**%**	**n**	**%**	**n**	**%**
Day 1 Post-infusion	x	x	x	x	x	x
Day 2	x	x	x	x	x	x
Day 5	x	x	x	x	x	x
Day 8	x	x	x	x	x	x

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b.
n=Number of subjects with missing data.

Table 26: DOOR Probability and 95% Confidence Interval by Day 8 – ITT Population, Stage 2a and 2b

Subjects With Non-missing DOOR – n (%)	Subjects With Missing DOOR – n (%)	DOOR Probability With IPW[a] (95% CI)[b]	DOOR Probability Without IPW[c] (95% CI)[b]
x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)

[a]Probability of more desirable DOOR in IV bacteriophage + 0.5 (probability of equal DOOR) using the greatest reduction in *P. aeruginosa* CFU/mL by Day 8. This analysis uses IPW to handle the impact of missing values of DOOR.
[b]95% CI calculated using the method in Halperin et. al Superiority of IV bacteriophage vs. placebo is concluded if the lower bound of the 95% CI for the DOOR probability is above 0.5.
[c]This calculation does not use inverse probability weighting to handle missing DOOR values.

Table 27: Sensitivity Analysis of DOOR by Day 8 – ITT Population, Stage 2a and 2b

	Imputed DOOR Ranks in IV Bacteriophage					
Imputed DOOR Ranks in Placebo	**1:0%, 2:0%, 3:0%, 4:100%**	**1:0%, 2:0%, 3:40%, 4:60%**	**1:20%, 2:20%, 3:40%, 4:20%**	**1:20%, 2:40%, 3:20%, 4:20%**	**1:60%, 2:40%, 3:0%, 4:0%**	**1:100%, 2:0%, 3:0%, 4:0%**
1:0%, 2:0%, 3:0%, 4:100%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
1:0%, 2:0%, 3:40%, 4:60%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
1:20%, 2:20%, 3:40%, 4:20%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
1:20%, 2:40%, 3:20%, 4:20%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
1:60%, 2:40%, 3:0%, 4:0%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
1:100%, 2:0%, 3:0%, 4:0%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)

Note: Values shown are the DOOR probability, i.e., the probability of more desirable DOOR in IV bacteriophage arm + 0.5 (probability of equal DOOR) using the greatest reduction in *P. aeruginosa* CFU/mL by Day 8, and the associated 95% CI obtained through the method described in Halperin et. al.

Table 28: Distribution of DOOR Categories by Treatment Group and Time Point – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	DOOR Rank	Selected IV Bacteriophage Dose (N=X)		Placebo (N=X)	
		n	%	n	%
Day 1 Post-infusion	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Day 2	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Day 5	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Day 8	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	Xx
	Missing	x	xx	x	xx
Maximum[a]	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	Xx
	Any Rank	x	xx	x	xx

Notes: N=Number of subjects in the ITT Population in Stage 2a and 2b.
n=Number of subjects in the corresponding analysis population, treatment group, and DOOR rank
[a]Maximum rows show DOOR ranks using greatest log_{10} reduction in *P. aeruginosa* CFU/mL by Day 8.

Table 29: Subgroup Analysis of DOOR at Day 8 – ITT Population, Stage 2a and 2b

[Implementation note: 'Organism X' will be replaced with any organisms recovered on sputum cultures with one yes/no row for each organism.]

Subgroup	Subjects With Non-missing DOOR – n_b (%)	Subjects With Non-missing DOOR – n_p (%)	Subjects With Missing DOOR – n_b (%)	Subjects With Missing DOOR – n_p (%)	DOOR Probability With IPW[a] (95% CI)[b]	DOOR Probability Without IPW[c] (95% CI)[b]
Susceptible to Bacteriophages – Yes	x (x)	x (x)	x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Susceptible to Bacteriophages – No	x (x)	x (x)	x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Presence of Co-infection with Organism X – Yes	x (x)	x (x)	x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Presence of Co-infection with Organism X – No	x (x)	x (x)	x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)

Notes: n_b=number of subjects in the ITT population in Stage 2a and 2b who received IV bacteriophage within the subgroup category. n_p=number of subjects in the ITT population who received placebo within the subgroup category. Denominator for percentages is the total number of IV bacteriophage subjects in the ITT population for n_b and the total number of placebo subjects in the ITT population for n_p.

[a]Probability of more desirable DOOR in IV bacteriophage arm + 0.5 (Probability of Equal DOOR) using the greatest reduction in *P. aeruginosa* CFU/mL by Day 8. This analysis uses IPW to handle the impact of missing values of DOOR.

[b]95% CI calculated using the method in Halperin et. al. Superiority of IV bacteriophage vs placebo is concluded if the lower bound of the 95% CI for the DOOR probability is above 0.5.

[c]This calculation does not use inverse probability weighting to handle missing DOOR values.

Table 30: Distribution of DOOR Categories by Subgroup, Treatment Group, and Time Point – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.]

Subgroup	DOOR Rank	Selected IV Bacteriophage Dose (N=X)		Placebo (N=X)	
		n	%	n	%
Day 1 Post-infusion					
Susceptible to Bacteriophages - Yes	Any Rank				
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Susceptible to Bacteriophages - No	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Presence of Co-infection with Organism X - Yes	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx

Table 30: Distribution of DOOR Categories by Subgroup, Treatment Group, and Time Point – ITT Population, Stage 2a and 2b *(continued)*

Subgroup	DOOR Rank	Selected IV Bacteriophage Dose (N=X)		Placebo (N=X)	
		n	%	n	%
Presence of Co-infection with Organism X - No	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Day 2					
…					
Day 5					
…		x	xx	x	xx
Day 8					
…		x	xx	x	Xx
Maximum[a]					
…					

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b in the given treatment group.
n=Number of subjects in the corresponding analysis population, treatment group, and DOOR rank.
[a]Maximum rows show DOOR ranks using greatest log_{10} reduction in *P. aeruginosa* CFU/mL by Day 8.

Table 31: Cumulative Proportions of DOOR Categories - ITT Analysis Population, Stage 2a and 2b

[Implementation note: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	DOOR Rank	Selected IV Bacteriophage Dose (N=X)			Placebo (N=X)	
		n (%)	Cumulative n (%)[a]	Cumulative Dichotomized Pr(DOOR)[a,b] (95% CI)[c]	n (%)	Cumulative n (%)[a]
Day 1 Post-infusion	Rank 1: No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	-	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-
Day 2	Rank 1: No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	-	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-
Day 5	Rank 1: No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-
Day 8	Rank 1: No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	-	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-

Table 31: Cumulative Proportions of DOOR Categories - ITT Analysis Population, Stage 2a and 2b *(continued)*

Maximum[d]	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	-	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-

Notes: N=Number of subjects in the ITT Population in the given treatment group.
n=Number of subjects in the corresponding analysis population, treatment group, and DOOR rank
[a]Cumulative n and percent do not include missing data.
[b]Probability of more desirable DOOR rank in IV Bacteriophage arm at each respective day + 0.5(Probability of Equal DOOR rank).
[c]95% CI calculated using the method in Halperin et. al.
[d]Maximum rows show DOOR ranks using greatest log_{10} reduction in *P. aeruginosa* CFU/mL by Day 8.

Table 32: Difference in Mean Partial Credit for DOOR Categories Through Day 8 – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis. The 95% CI for the difference in means is computed from Welch's t-test]

Scenario	Time Point	Treatment Group	n	Mean (SD)	Difference in Means (95% CI)[a]
A: (1=100, 2=100, 3=100, 4=0)	Day 1 Post-infusion	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
	Day 2	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
	Day 5	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
	Day 8	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
	Maximum	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
[Extend the table to add Scenarios **B: (1=100, 2=100, 3=0, 4=0) and C: (1=100, 2=0, 3=0, 4=0)]**					

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b.
n=Number of subjects in the corresponding analysis population with non-missing values of partial credit scores.
SD=Standard Deviation.
[a]The 95% CI for the difference in means is computed from Welch's t-test.

Table 33: Summary of DOOR Components Through Day 8 - ITT Analysis Population, Stage 2a and 2b

[Implementation note: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.]

DOOR Component	Selected IV Bacteriophage Dose (N=X)			Placebo (N=X)	
	n (%)	Cumulative n (%)	Cumulative Dichotomized Pr(DOOR)[a] (95% CI)[b]	n (%)	Cumulative n (%)
Day 1 Post-infusion SAE					
No SAE (related to study product)	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
SAE	x (x)	x (x)	-	x (x)	x (x)
DOOR Probability for SAE Component[c]	x (100)	x (100)	x.x (x.x, x.x)	x (100)	x (100)
log10 Reduction in *P. aeruginosa* CFU/mL					
>2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
<1 $\log_{10}$ reduction/increase in *P. aeruginosa* CFU/mL	x (x)	x (x)	-	x (x)	x (x)
DOOR Probability for log10 Reduction in *P. aeruginosa* CFU/mL Component	x (100)	x (100)	x.x (x.x, x.x)	x (100)	x (100)
Day 2					
…					
Day 5					
…					
Day 8					
…					
Maximum[d]					
…					

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b with sputum collected at the given time point.
n=Number of subjects in the corresponding analysis population, treatment group, and DOOR category at the given time point.
[a]Probability of more desirable DOOR component rank in IV Bacteriophage arm at each respective day + 0.5(Probability of Equal DOOR component rank). Dichotomized Pr(DOOR) of multiclass DOOR components classify the respective row class and more desirable classes (if any) as equally desirable.
[b]95% CI calculated using the method in Halperin et. al.
[c]Becasue the SAE Component is dichotomous, the DOOR Probability for that component and the Cumulative Dichotomized Pr(DOOR) should be equal.
[d]Maximum rows show DOOR ranks using greatest $\log_{10}$ reduction in *P. aeruginosa* CFU/mL by Day 8.

Table 34: Absolute Change in FEV1 from Baseline by Treatment Group – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected Dose' will be replaced with the dose chosen by the interim analysis].

Time Point	Treatment Group	FEV1 (liters)					Change from Baseline (liters)					
		n	Mean	SD	Median	Min, Max	n	Mean	SD	Median	Min, Max	95% CI[a]
Baseline	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	-	-	-	-	-	-
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	-	-	-	-	-	-
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	x.xx, x.xx
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	x.xx, x.xx
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	x.xx, x.xx
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	x.xx, x.xx
Maximum	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	x.xx, x.xx

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b.
n=Number of subjects in the ITT Population with non-missing FEV1 measurements at the time point of interest. For the change from baseline, n represents the number of subjects in the ITT population with non-missing values at baseline and at the time point being assessed.
SD=Standard Deviation
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
[a]95%CI is calculated from a t-distribution.

Table 35: Percent Change in Predicted FEV1 from Baseline by Treatment Group – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected Dose' will be replaced with the dose chosen by the interim analysis].

Time Point	Treatment Group	Percent Change in Predicted FEV1 (Mean (SD))
Day 1 Post-infusion	Selected Dose (N=X)	xx (xx.x)
	Placebo (N=X)	xx (xx.x)
Day 2	Selected Dose (N=X)	xx (xx.x)
	Placebo (N=X)	xx (xx.x)
Day 5	Selected Dose (N=X)	xx (xx.x)
	Placebo (N=X)	xx (xx.x)
Day 30	Selected Dose (N=X)	xx (xx.x)
	Placebo (N=X)	xx (xx.x)
Maximum	Selected Dose (N=X)	xx (xx.x)
	Placebo (N=X)	xx (xx.x)

Note: N=Number of subjects in the ITT population in Stage 2a and 2b.
Baseline is defined as the last measurement taken prior to dosing on Study Day 1. Predicted FEV1 calculated using GLI global standards with a response threshold of 0.05.

Table 36: Change in log_{10} *P. aeruginosa* Colony Counts by Treatment Group and Morphology – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	Treatment Group	Colony Counts						Change from Baseline						
		n	Mean	SD	Median	Q1, Q3[a]	Min, Max	n	Mean	SD	Median	Min, Max	Q1, Q3[a]	95% CI[b]
[Morphology 1]														
Baseline	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	-	-	-	-	-	-
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	-	-	-	-	-	-
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Maximum	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	xx, xx	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
[Repeat for all morphologies]														

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b.
n=Number of subjects in the ITT population in Stage 2a and 2b with non-missing colony counts at the time point of interest. For the change from baseline, n represents the number of subjects in the ITT population with non-missing values at baseline and at the time point being assessed.
SD=Standard Deviation
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
[a]Q1 and Q3 represent the 25th and 75th percentiles, respectively
[b]95%CI is calculated from a t-distribution.

Table 37: Proportion of *P. aeruginosa* Isolates Susceptible to Individual Bacteriophages – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected Dose' will be replaced with the dose chosen by the interim analysis. If multiple timepoints are collected, then this table will be stratified by timepoint with an additional 'All Timepoints' category.]

***P. aeruginosa* Isolate**	**Selected IV Bacteriophage Dose**				**Placebo**				**Difference**
	N	**n**	**%**	**95% CI[a]**	**N**	**n**	**%**	**95% CI[a]**	**95% CI[b]**
[Bacteriophage 1]									
[Isolate 1]	x	x	x	(x.x, x.x)	x	x	x	(x.x, x.x)	xx (x.x, x.x)
[Isolate 2]	x	x	x	(x.x, x.x)	x	x	x	(x.x, x.x)	xx (x.x, x.x)
[Isolate 3]	x	x	x	(x.x, x.x)	x	x	x	(x.x, x.x)	xx (x.x, x.x)
[Isolate 4]	x	x	x	(x.x, x.x)	x	x	x	(x.x, x.x)	xx (x.x, x.x)
[Repeat for each bacteriophage]									

Notes: *P. aeruginosa* isolate will be identified by individual morphotype ID.
N=Number of subjects in the ITT population in Stage 2a and 2b with non-missing values for isolate susceptibility.
n=Number of subjects with isolates susceptible to the corresponding bacteriophage.
[a]95% CI for proportions calculated using the Wilson method.
[b]95% CI for the difference in proportions, IV bacteriophage relative to placebo, calculated using the Miettinen–Nurminen method.

Table 38: Change from Baseline of QoL Score, CFQ-R Questionnaire – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected Dose' will be replaced with the dose chosen by the interim analysis.

The following domains will be included: Physical, Role, Vitality, Emotion, Social, Body, Eat, Treat, Health, Weight, Respiration, Digestion, Sinus, and Overall. The Overall score for each subject will be calculated as the sum of the combined domain scores.]

Time Point	Treatment Group	QoL Score					Change from Baseline					
		n	Mean	SD	Median	Min, Max	n	Mean	SD	Median	Min, Max	95% CI[a]
Physical												
Baseline	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	-	-	-	-	-	-
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	-	-	-	-	-	-
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	x.xx, x.xx
…												
[Repeat for all domains]												

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b.
n=Number of subjects in the ITT population in Stage 2a and 2b with non-missing QoL scores at the time point of interest. For the change from baseline, n represents the number of subjects in the ITT population in Stage 2a and 2b with non-missing values at baseline and at the time point being assessed.
SD=Standard Deviation
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
[a]95% CI will be calculated from a t-distribution.

Table 39: Change from Baseline of QoL Score, CFRSD Questionnaire – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	Treatment Group	Total QoL Score					Change from Baseline					
		n	Mean	SD	Median	Min, Max	n	Mean	SD	Median	Min, Max	95% CI[a]
Baseline	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	-	-	-	-	-	-
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	-	-	-	-	-	-
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	x.xx, x.xx
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	x.xx, x.xx
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx	xx.x	xx.x	xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx	xx.x	xx.x	xx	xx, xx	x.xx, x.xx
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx	xx.x	xx.x	xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	x.xx, x.xx
Maximum	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx	xx.x	xx.x	xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	x.xx, x.xx

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b.
n=Number of subjects in the ITT population in Stage 2a and 2b with non-missing QoL score at the time point of interest. For the change from baseline, n represents the number of subjects in the ITT population in Stage 2a and 2b with non-missing values at baseline and at the time point being assessed.
SD=Standard Deviation
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
[a]95% CI is calculated from a t-distribution.

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 40: Overall Summary of Adverse Events

Subjects meeting at least one of the below conditions	$4x10^7$ PFU Dose (N=X)		$4x10^8$ PFU Dose (N=X)		$4x10^9$ PFU Dose (N=X)		Placebo (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	n	%
Stage 1										
At least one adverse event	x	xx	x	xx	x	x	x	xx	x	xx
At least one related adverse event	x	x	x	x	x	x	x	x	x	x
At least one mild (or worse) related adverse event	x	x	x	x	x	x	x	x	x	x
At least one moderate (or worse) related adverse event	x	x	x	x	x	x	x	x	x	x
At least one severe related adverse event	x	x	x	x	x	x	x	x	x	x
At least one serious adverse event	x	x	x	x	x	x	x	x	x	x
At least one related, serious adverse event	x	x	x	x	x	x	x	x	x	x
At least one adverse event leading to early termination	x	x	x	x	x	x	x	x	x	x
Stage 2a										
…										
Stage 2a and 2b										
…										

Note: N=Number of subjects in the Safety Population

Table 41: Adverse Events Occurring in 5% of Subjects in Any Treatment Group by MedDRA System Organ Class, High Level Term, Preferred Term, and Treatment Group, Stage 1 – Safety Population

MedDRA System Organ Class	MedDRA High Level Term	MedDRA Preferred Term	$4x10^7$ PFU Dose (N=X)			$4x10^8$ PFU Dose (N=X)			$4x10^9$ PFU Dose (N=X)			Placebo (N=X)			All Subjects (N=X)		
			n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events
Serious Adverse Events																	
All	All	All	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
SOC1	HLT1	PT1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Etc.	Etc.	Etc.															
Other (Non-serious) Adverse Events																	
All	All	All	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
SOC1	HLT1	PT1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Etc	Etc.	Etc															

Notes: N=Number of subjects in the Safety Population.
n=Number of subjects reporting event.
Events=Total frequency of events reported.

Table 42: Adverse Events Occurring in 5% of Subjects in Any Treatment Group by MedDRA System Organ Class, Preferred Term, and Treatment Group, Stage 2a – Safety Population

Table 43: Adverse Events Occurring in 5% of Subjects in Any Treatment Group by MedDRA System Organ Class, Preferred Term, and Treatment Group, Stage 2a and 2b – Safety Population

Table 44: Summary of Grade 2 or Higher Treatment Emergent AEs by MedDRA System Organ Class, High Level Term, Preferred Term, and Treatment Group – ITT Population

[Implementation Note: If there is only 1 PT for an SOC, there will be no "Any PT" row.

Treatment group order: All subjects, 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, 4 x 10^9 PFU Dose, Placebo]

Treatment Group	MedDRA System Organ Class	MedDRA High Level Term	MedDRA Preferred Term	N	n (%)	95% CI[a]	Number of Events
All Subjects (N=X)	Any SOC	Any HLT	Any PT	x	x (x)	xx, xx	x
	[SOC 1]	Any HLT	Any PT	x	x (x)	xx, xx	x
		[HLT 1]	Any PT	x	x (x)	xx, xx	x
			[PT 1]	x	x (x)	xx, xx	x
	[SOC 2]	Any HLT	Any PT	x	x (x)	xx, xx	x
		[HLT 1]	Any PT	x	x (x)	xx, xx	x
			[PT 1]	x	x (x)	xx, xx	x
4x10^7 PFU Dose (N=X)	…		…	x	x (x)	xx, xx	x
	…		…	x	x (x)	xx, xx	x
Placebo (N=X)	…		…	x	x (x)	xx, xx	x

Notes: N=Number of subjects in the ITT population in the specified Treatment Group.
n=Number of subjects with Grade 2 or higher treatment-emergent AEs.
A subject is only counted once per PT per treatment group and study part.
[a] Exact Clopper-Pearson Confidence Interval.

Table 45: Difference in Proportion of Grade 2 or Higher Treatment Emergent AEs in IV Bacteriophage vs. Placebo – ITT Population

[Implementation Note: If there is only 1 PT for an SOC, there will be no "Any PT" row. This table will compare the Selected Dose of IV Bacteriophage to Placebo.]

MedDRA System Organ Class	MedDRA High Level Term	MedDRA Preferred Term	IV Bacteriophage n(%)	Placebo n(%)	Difference in Proportion	95% CI[a]
Any SOC	Any HLT	Any PT	x (x)	x (x)	x	xx, xx
[SOC 1]	Any HLT	Any PT	x (x)	x (x)	x	xx, xx
	[HLT 1]	Any PT	x (x)	x (x)	x	xx, xx
		[PT 1]	x (x)	x (x)	x	xx, xx
[SOC 2]	Any HLT	Any PT	x (x)	x (x)	x	xx, xx
	[HLT 1]	Any PT	x (x)	x (x)	x	xx, xx
		[PT 1]	x (x)	x (x)	x	xx, xx
…		…	x (x)	x (x)	x	xx, xx
…		…	x (x)	x (x)	x	xx, xx
…		…	x (x)	x (x)	x	xx, xx

Notes: n=Number of subjects with Grade 2 or higher treatment-emergent AEs.
A subject is only counted once per PT per treatment group and study part.
[a] 95% CI for the difference in proportions, IV bacteriophage relative to placebo, calculated using the Miettinen–Nurminen method.

14.3.1.2 Unsolicited Adverse Events

Table 46: Summary of Unsolicited Adverse Events by MedDRA System Organ Class, High Level Term, Preferred Term, and Treatment Group, Stage 1 – Safety Population

[Implementation Note: If there is only 1 PT for an SOC, there will be no "Any PT" row.

Treatment group order: All subjects, 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, 4 x 10^9 PFU Dose, Placebo.]

Treatment Group	MedDRA System Organ Class	MedDRA High Level Term	MedDRA Preferred Term	N	n (%)	95% CI[a]	Number of Events
All Subjects (N=X)	Any SOC	Any HLT	Any PT	x	x (x)	xx, xx	x
	[SOC 1]	Any HLT	Any PT	x	x (x)	xx, xx	x
		[HLT 1]	Any PT	x	x (x)	xx, xx	x
			[PT 1]	x	x (x)	xx, xx	x
	[SOC 2]	Any HLT	Any PT	x	x (x)	xx, xx	x
		[HLT 1]	Any PT	x	x (x)	xx, xx	x
			[PT 1]	x	x (x)	xx, xx	x
4x10^7 PFU Dose (N=X)	…		…	x	x (x)	xx, xx	x
…	…		…	x	x (x)	xx, xx	x
Placebo (N=X)	…		…	x	x (x)	xx, xx	x

Notes: N=number of subjects in the Safety Population in the specified Treatment Group.
A subject is only counted once per PT per treatment group and study part.
[a] Exact Clopper-Pearson Confidence Interval.

Table 47: Summary of Unsolicited Adverse Events by MedDRA System Organ Class, Preferred Term, and Treatment Group, Stage 2a – Safety Population

Table 48: Summary of Unsolicited Adverse Events by MedDRA System Organ Class, Preferred Term, and Treatment Group, Stage 2a and 2b – Safety Population

Table 49: Unsolicited Adverse Events by MedDRA System Organ Class, High Level Term, Preferred Term, Maximum Severity, Relationship, and Treatment Group, Stage 1 – Safety Population

[Implementation Note: Treatment group order: All subjects, 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, 4 x 10^9 PFU Dose, Placebo.]

Treatment Group	MedDRA System Organ Class	MedDRA High Level Term	MedDRA Preferred Term	Severity	Related n (%)	Not Related n (%)	Total n (%)
All Subjects (N=X)	Any SOC	Any HLT	Any PT	Any Severity	x (%)	x (%)	x (%)
				Mild	x (%)	x (%)	x (%)
				Moderate	x (%)	x (%)	x (%)
				Severe	x (%)	x (%)	x (%)
	[SOC 1]	Any HLT	Any PT	Any Severity	x (%)	x (%)	x (%)
				…	x (%)	x (%)	x (%)
			[PT 1]	Any Severity	x (%)	x (%)	x (%)
				…	x (%)	x (%)	x (%)
4x10^7 PFU Dose (N=X)	Any SOC		Any PT	Any Severity	x (%)	x (%)	x (%)
…	…		…	…	x (%)	x (%)	x (%)
Placebo (N=X)	…		…	…	x (%)	x (%)	x (%)

Notes: N=Number of subjects in the Safety Population in each Treatment Group.
Subjects are only counted once per PT and treatment group, in the highest reported severity.

Table 50: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group, Stage 2a – Safety Population

Table 51: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group, Stage 2a and 2b – Safety Population

Table 52: Summary of TEAEs, On-Therapy SAEs, and AEs Leading to Discontinuation by MedDRA Preferred Term, and Treatment Group, Stage 1 – Safety Population

[Implementation note: Sort this table by decreasing frequency for 'All Subjects'.]

Preferred Term	$4x10^7$ PFU Dose (N=X)			$4x10^8$ PFU Dose (N=X)			$4x10^9$ PFU Dose (N=X)			Placebo (N=X)			All Subjects (N=X)		
	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events
Treatment-Emergent AEs															
All	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
PT1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
PT2	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Etc	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
…	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
On-Therapy AEs															
…	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
AEs Leading to Discontinuation															

Note: N=Number of subjects in the Safety Population.

Table 53: Summary of TEAEs, On-Therapy SAEs, and AEs Leading to Discontinuation by MedDRA Preferred Term, and Treatment Group, Stage 2a – Safety Population

Table 54: Summary of TEAEs, On-Therapy SAEs, and AEs Leading to Discontinuation by MedDRA Preferred Term, and Treatment Group, Stage 2a and 2b – Safety Population

Table 55: Summary of Fatal On-Therapy SAEs by MedDRA Preferred Term, and Treatment Group – Safety Population

[Implementation note: Sort this table by decreasing frequency for 'All Subjects'.]

Preferred Term	$4x10^7$ PFU Dose (N=X)			$4x10^8$ PFU Dose (N=X)			$4x10^9$ PFU Dose (N=X)			Placebo (N=X)			All Subjects (N=X)		
	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events
Stage 1															
All	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
PT1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
PT2	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Etc															
Stage 2a															
…															
Stage 2a and 2b															
…															

Note: N=Number of subjects in the Safety Population.

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 56: Listing of Serious Adverse Events

Adverse Event	No. of Days Post Associated Dose (Duration)	No. of Days Post Dose the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA High Level Term	MedDRA Preferred Term
Subject ID:, Treatment Group:, AE Number:												
Comments:												
Subject ID:, Treatment Group:, AE Number:												
Comments:												

Table 57: Listing of Adverse Events of Special Interest

This table will be similar to Table 46.

[Implementation note: Exclude 'No days post dose event became serious', 'Reason reported as an SAE' columns.]

Table 58: Listing of Adverse Events Leading to Discontinuation

This table will be similar to Table 46.

[Implementation note: Exclude 'No days post dose event became serious', 'Reason reported as an SAE' and 'Subject discontinued due to AE' columns.]

Table 59: Listing of Subjects Whose Outcome was Fatal During the Study

This table will be similar to Table 46.

[Implementation note: Exclude 'No days post dose event became serious', 'Reason reported as an SAE', 'Subject discontinued due to AE', and 'Action taken with study treatment' columns.]

14.3.3 Narratives of Deaths, Other Serious and Significant Adverse Events

(Not included in SAP, but this is a placeholder for the CSR)

14.3.4 Abnormal Laboratory Value Listings (by Subject)

Table 60: Listing of Abnormal Laboratory Results - Chemistry

[Implementation Note: This listing is included in the table shells document, as it is included in the body of the CSR. This listing should include all hematology results for any subject that had at least one abnormal chemistry laboratory result. A complete listing of all laboratory results is included in the listings document. In the Laboratory Parameter column, indicate the units after the parameter, e.g., Hemoglobin (g/dL). This listing is not color-coded, but the severity should be included in parentheses after the result, e.g., 16.2 (mild). In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification.]

Subject ID	Treatment Group	Sex	Age (years)	Planned Time Point	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Relationship to Treatment	If Not Related, Alternate Etiology	Action Taken with Study Treatment	Subject Discontinued Due to Result?

Table 61: Listing of Abnormal Laboratory Results - Hematology

[Implementation Note: This listing is included in the table shells document, as it is included in the body of the CSR. This listing should include all hematology results for any subject that had at least one abnormal hematology laboratory result. A complete listing of all laboratory results is included in the listings document. In the Laboratory Parameter column, indicate the units after the parameter, e.g., Hemoglobin (g/dL).This listing is not color-coded, but the severity should be included in parentheses after the result, e.g., 16.2 (mild).In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification.]

Subject ID	Treatment Group	Sex	Age (years)	Planned Time Point	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Relationship to Treatment	If Not Related, Alternate Etiology	Action Taken with Study Treatment	Subject Discontinued Due to Result?

Table 62: Listing of Abnormal Laboratory Results – Liver Function Tests

[Implementation Note: This listing is included in the table shells document, as it is included in the body of the CSR. This listing should include all urinalysis results for any subject that had at least one abnormal urinalysis laboratory result. A complete listing of all laboratory results is included in the listings document. In the Laboratory Parameter column, indicate the units after the parameter, e.g., Hemoglobin (g/dL). This listing is not color-coded, but the severity should be included in parentheses after the result, e.g., 16.2 (mild).In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification.]

Subject ID	Treatment Group	Sex	Age (years)	Planned Time Point	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Relationship to Treatment	If Not Related, Alternate Etiology	Action Taken with Study Treatment	Subject Discontinued Due to Result?

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Table 63: Chemistry Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter

[Implementation note: If no missing or outside normal range (ONR) results are reported, these columns will not be included, and corresponding footnotes should be removed. If parameter is not graded then only 'Within Normal Range', 'Outside Normal Range', and 'Missing' columns will be included.

Treatment group order: All subjects, 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, 4 x 10^9 PFU Dose, Placebo.]

Time Point	Treatment Group	N	None		Outside Normal Range[a]		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Stage 1														
Baseline	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
	Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Day 2	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
Day 5	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
Day 8	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
Day 12[b]	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
Day 30	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
Max Severity Post Baseline	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													

Table 63: Chemistry Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter *(continued)*

Time Point	Treatment Group	N	None		Outside Normal Range[a]		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Stage 2a														
…														
Stage 2a and 2b														
…														

Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N=Number of subjects in the Safety Population
[a]Post-dose measurements that were outside the normal range but did not meet the definition for an AE due to the value being less than or equal to the measurement at baseline will be categorized as "Outside Normal Range"
[b]Only data from Stage 1 subjects will be summarized for this visit. Any Stage 2a subjects with Day 12 data will be included only in lab listings.

Tables with similar format:

Table 64: Chemistry Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Serum Creatinine

Table 65: Chemistry Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Blood Urea Nitrogen (BUN)

Table 66: Chemistry Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Glucose

Table 67: Chemistry Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Sodium

Table 68: Chemistry Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Potassium

Table 69: Chemistry Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Chloride

Table 70: Chemistry Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Bicarbonate

Table 71: Chemistry Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Calcium

Table 72: Chemistry Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Serum Creatinine

[Implementation note: Treatment group order: All subjects, 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, 4 x 10^9 PFU Dose, Placebo.]

Time Point	Treatment Group	Laboratory Value (Units)					Change from Baseline (Units)				
		n	Mean	Standard Deviation	Median	Min, Max	n	Mean	Standard Deviation	Median	Min, Max
Stage 1											
Baseline	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	-	-	-	-	-
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	-	-	-	-	-
Day 2	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 5	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 8	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 12[a]	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 30	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx

Table 72: Chemistry Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Serum Creatinine *(continued)*

Time Point	Treatment Group	Laboratory Value (Units)					Change from Baseline (Units)				
		n	Mean	Standard Deviation	Median	Min, Max	n	Mean	Standard Deviation	Median	Min, Max
Stage 2a											
…											
Stage 2a and 2b											
…											

Notes: N=Number of subjects in the Safety Population.
n=Number of subjects in the Safety Population with non-missing laboratory values at the time point of interest. For the change from baseline, n represents the number of subjects in the Safety Population with non-missing values at baseline and at the time point being assessed.
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
[a]Only data from Stage 1 subjects will be summarized for this visit. Any Stage 2a subjects with Day 12 data will be included only in lab listings.

Tables with similar format:

Table 73: Chemistry Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Blood Urea Nitrogen

Table 74: Chemistry Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Glucose

Table 75: Chemistry Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Sodium

Table 76: Chemistry Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Potassium

Table 77: Chemistry Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Chloride

Table 78: Chemistry Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Bicarbonate

Table 79: Chemistry Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Calcium

14.3.5.2 Hematology Results

Table 80: Hematology Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter

[Implementation note: If no missing or ONR results are reported these columns will not be included and corresponding footnote will be removed. If parameter is not graded then only 'Within Normal Range', 'Outside Normal Range', and 'Missing' columns will be included].

Treatment group order: All subjects, 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, 4 x 10^9 PFU Dose, Placebo.]

Time Point	Treatment Group	N	None		Outside Normal Range[a]		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Stage 1														
Baseline	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
	Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Day 2	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
Day 5	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
Day 8	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
Day 12[b]	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
Day 30	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
Max Severity Post Baseline	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													

Table 80: Hematology Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter *(continued)*

Time Point	Treatment Group	N	None		Outside Normal Range[a]		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Stage 2a														
…														
Stage 2a and 2b														
…														

Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N=Number of subjects in the Safety Population
[a]Post-dose measurements that were outside the normal range but did not meet the definition for an AE due to the value being less than or equal to the measurement at baseline will be categorized as "Outside Normal Range"
[b]Only data from Stage 1 subjects will be summarized for this visit. Any Stage 2a subjects with Day 12 data will be included only in lab listings.

Tables with similar format:

Table 81: Hematology Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – RBC

Table 82: Hematology Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Hemoglobin

Table 83: Hematology Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Hematocrit

Table 84: Hematology Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – WBC

Table 85: Hematology Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Platelets

Table 86: Hematology Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Neutrophils

Table 87: Hematology Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Lymphocytes

Table 88: Hematology Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Monocytes

Table 89: Hematology Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – RBC

[Implementation note: Treatment group order: All subjects, 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, 4 x 10^9 PFU Dose, Placebo.]

Time Point	Treatment Group	Laboratory Value (Units)					Change from Baseline (Units)				
		n	Mean	Standard Deviation	Median	Min, Max	n	Mean	Standard Deviation	Median	Min, Max
Stage 1											
Baseline	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	-	-	-	-	-
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	-	-	-	-	-
Day 2	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 5	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 8	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 12[a]	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 30	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx

Table 89: Hematology Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – RBC *(continued)*

Time Point	Treatment Group	Laboratory Value (Units)					Change from Baseline (Units)				
		n	Mean	Standard Deviation	Median	Min, Max	n	Mean	Standard Deviation	Median	Min, Max
Stage 2a											
…											
Stage 2a and 2b											
…											

Notes: N=Number of subjects in the Safety Population.
n=Number of subjects in the Safety Population with non-missing laboratory values at the time point of interest. For the change from baseline, n represents the number of subjects in the Safety population with non-missing values at baseline and at the time point being assessed.
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
[a]Only data from Stage 1 subjects will be summarized for this visit. Any Stage 2a subjects with Day 12 data will be included only in lab listings.

Tables with similar format:

Table 90: Hematology Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Hemoglobin

Table 91: Hematology Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Hematocrit

Table 92: Hematology Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – WBC

Table 93: Hematology Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Platelets

Table 94: Hematology Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Neutrophils

Table 95: Hematology Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Lymphocytes

Table 96: Hematology Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Monocytes

14.3.5.3 Liver Function Results

Table 97: Liver Function Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Liver Function Parameter

[Implementation note: If no missing or ONR results are reported these columns will not be included and the corresponding footnote will be removed. If parameter is not graded then only 'Within Normal Range', 'Outside Normal Range', and 'Missing' columns will be included].

Treatment group order: All subjects, 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, 4 x 10^9 PFU Dose, Placebo.]

Time Point	Treatment Group	N	None		Outside Normal Range[a]		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Stage 1														
Baseline	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	…													
	Placebo													
Day 2	All Subjects (N=X)													
	…													
Day 5	All Subjects (N=X)													
	…													
Day 8	All Subjects (N=X)													
	…													
Day 12[b]	All Subjects (N=X)													
	…													
Day 30	All Subjects (N=X)													
	…													
Max Severity Post Baseline	All Subjects (N=X)													
	…													

Table 97: Liver Function Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Liver Function Parameter *(continued)*

Time Point	Treatment Group	N	None		Outside Normal Range[a]		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Stage 2a														
…														
Stage 2a and 2b														
…														

Notes: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments. N=Number of subjects in the Safety Population. [a]Post-dose measurements that were outside the normal range but did not meet the definition for an AE due to the value being less than or equal to the measurement at baseline will be categorized as "Outside Normal Range"
[b]Only data from Stage 1 subjects will be summarized for this visit. Any Stage 2a subjects with Day 12 data will be included only in lab listings.

Tables with similar format:

Table 98: Liver Function Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Aspartate Aminotransferase

Table 99: Liver Function Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Alanine Aminotransferase

Table 100: Liver Function Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Alkaline Phosphatase

Table 101: Liver Function Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Total Bilirubin

Table 102: Liver Function Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Albumin

Table 103: Liver Function Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Lactate Dehydrogenase

Table 104: Liver Function Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Total Protein

Table 105: Liver Function Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Aspartate Aminotransferase

[Implementation note: Treatment group order: All subjects, 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, 4 x 10^9 PFU Dose, Placebo.]

Time Point	Treatment Group	Laboratory Value (Units)					Change from Baseline (Units)				
		n	Mean	Standard Deviation	Median	Min, Max	n	Mean	Standard Deviation	Median	Min, Max
Stage 1											
Baseline	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	-	-	-	-	-
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	-	-	-	-	-
Day 2	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 5	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 8	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 12[a]	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 30	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx

Table 105: Liver Function Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Aspartate Aminotransferase *(continued)*

Time Point	Treatment Group	Laboratory Value (Units)					Change from Baseline (Units)				
		n	Mean	Standard Deviation	Median	Min, Max	n	Mean	Standard Deviation	Median	Min, Max
Stage 2a											
…											
Stage 2a and 2b											
…											

Notes: N=Number of subjects in the Safety Population.
n=Number of subjects in the Safety Population with non-missing laboratory values at the time point of interest. For the change from baseline, n represents the number of subjects in the Safety Population with non-missing values at baseline and at the time point being assessed.
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
[a]Only data from Stage 1 subjects will be summarized for this visit. Any Stage 2a subjects with Day 12 data will be included only in lab listings.

Tables with similar format:

Table 106: Liver Function Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Alanine Aminotransferase

Table 107: Liver Function Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Alkaline Phosphatase

Table 108: Liver Function Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Total Bilirubin

Table 109: Liver Function Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Albumin

Table 110: Liver Function Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Lactate Dehydrogenase

Table 111: Liver Function Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Total Protein

14.3.6 Displays of Vital Signs

Table 112: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Any Assessment

[Implementation note: Treatment group order: All subjects, 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, 4 x 10^9 PFU Dose, Placebo.]

Time Point	Treatment Group	N	None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Stage 1												
Baseline	All Subjects (N=X)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	…											
	Placebo	x	xx	x	xx	x	xx	x	xx	x	xx	x
Day 2	All Subjects (N=X)	x	xx	x	xx	x	xx	x	xx	x	xx	x
	…											
Day 5	All Subjects (N=X)	x	xx	x	xx	x	xx	x	xx	x	xx	x
	…											
Day 8	All Subjects (N=X)	x	xx	x	xx	x	xx	x	xx	x	xx	x
	…											
Day 12[a]	All Subjects (N=X)	x	xx	x	xx	x	xx	x	xx	x	xx	x
	…											
Day 30	4x10^7 PFU Dose (N=X)	x	xx	x	xx	x	xx	x	xx	x	xx	x
	…											
Max Severity Post Baseline	All Subjects (N=X)	x	xx	x	xx	x	xx	x	xx	x	xx	x
	…											
Stage 2a												
…												
Stage 2a and 2b												
…												

Notes: N=Number of subjects in the Safety Population.
n=Number of subjects in the Safety Population with non-missing vital sign values at the time point of interest.
[a]Only data from Stage 1 subjects will be summarized for this visit. Any Stage 2a subjects with Day 12 data will be included only in lab listings.

Table 112: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Any Assessment *(continued)*

Tables with similar format:

Table 113: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Systolic Blood Pressure

Table 114: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Diastolic Blood Pressure

Table 115: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Heart Rate

Table 116: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Respiratory Rate

Table 117: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Body Temperature

Table 118: Vital Signs Summary Statistics by Parameter, Time Point, and Treatment Group – Systolic Blood Pressure

[Implementation note: Treatment group order: All subjects, 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, 4 x 10^9 PFU Dose, Placebo.]

Time Point	Treatment Group	Vital Sign Value (Units)					Change from Baseline (Units)				
		n	Mean	Standard Deviation	Median	Min, Max	n	Mean	Standard Deviation	Median	Min, Max
Stage 1											
Baseline	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	-	-	-	-	-
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	-	-	-	-	-
Day 2	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 5	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 8	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 12[a]	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
Day 30	All Subjects (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	…										
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx

Table 118: Vital Signs Summary Statistics by Parameter, Time Point, and Treatment Group – Systolic Blood Pressure *(continued)*

Time Point	Treatment Group	Vital Sign Value (Units)					Change from Baseline (Units)				
		n	Mean	Standard Deviation	Median	Min, Max	n	Mean	Standard Deviation	Median	Min, Max
Stage 2a											
…											
Stage 2a and 2b											
…											

Notes: N=Number of subjects in the Safety Population.
n=Number of subjects in the Safety Population with non-missing laboratory values at the time point of interest. For the change from baseline, n represents the number of subjects in the Safety Population with non-missing values at baseline and at the time point being assessed.
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
[a]Only data from Stage 1 subjects will be summarized for this visit. Any Stage 2a subjects with Day 12 data will be included only in lab listings.

Tables with similar format:

Table 119: Vital Signs Summary Statistics by Parameter, Time Point, and Treatment Group – Diastolic Blood Pressure

Table 120: Vital Signs Summary Statistics by Parameter, Time Point, and Treatment Group – Heart Rate

Table 121: Vital Signs Summary Statistics by Parameter, Time Point, and Treatment Group – Respiratory Rate

Table 122: Vital Signs Summary Statistics by Parameter, Time Point, and Treatment Group – Body Temperature

14.4 Summary of Concomitant Medications

Table 123: Number and Percentage of Subjects with Prior Medications by WHO Drug Classification and Treatment Group, Stage 1

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	$4x10^7$ PFU Dose (N=X)		$4x10^8$ PFU Dose (N=X)		$4x10^9$ PFU Dose (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 1 – 1]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 1]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 2]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 3]	x	xx	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 – 2]	[ATC 2 - 1]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 2]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 3]	x	xx	x	xx	x	xx	x	xx	x	xx

Notes: N=Number of subjects in the Safety Population.
n=Number of subjects reporting taking at least one medication in the specific WHO Drug Class.

Tables with similar format:

Table 124: Number and Percentage of Subjects with Prior Medications by WHO Drug Classification and Treatment Group, Stage 2a

Table 125: Number and Percentage of Subjects with Prior Medications by WHO Drug Classification and Treatment Group, Stage 2a and 2b

Table 126: Number and Percentage of Subjects with Concurrent Medications by WHO Drug Classification and Treatment Group, Stage 1

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	$4x10^7$ PFU Dose (N=X)		$4x10^8$ PFU Dose (N=X)		$4x10^9$ PFU Dose (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 1 – 1]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 1]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 2]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 3]	x	xx	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 – 2]	[ATC 2 - 1]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 2]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 3]	x	xx	x	xx	x	xx	x	xx	x	xx

Notes: N=Number of subjects in the Safety Population.
n=Number of subjects reporting taking at least one medication in the specific WHO Drug Class.

Tables with similar format:

Table 127: Number and Percentage of Subjects with Concurrent Medications by WHO Drug Classification and Treatment Group, Stage 2a

Table 128: Number and Percentage of Subjects with Concurrent Medications by WHO Drug Classification and Treatment Group, Stage 2a and 2b

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9.1 Overall Study Design and Plan Description

Figure 1: Study Design

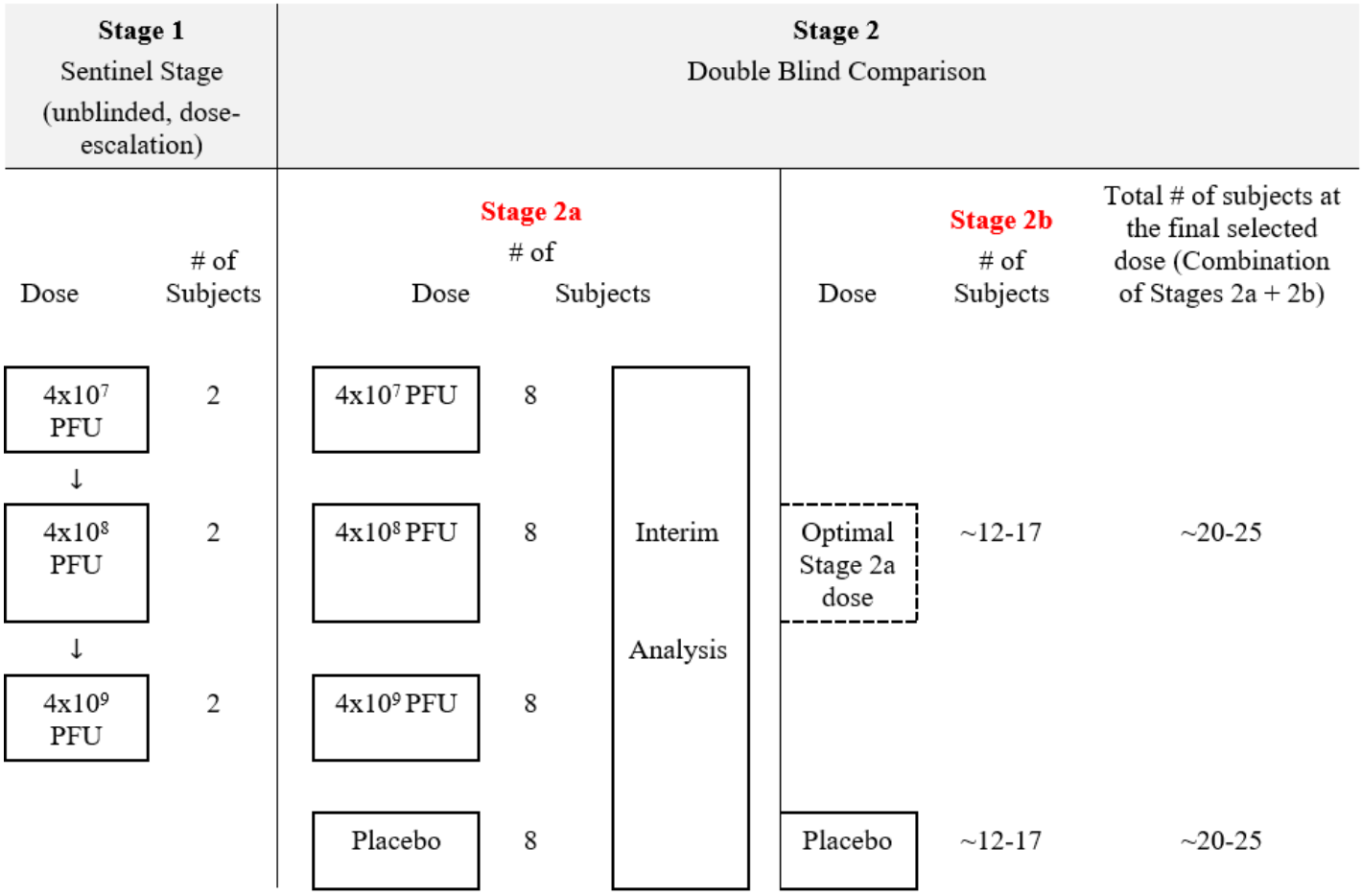
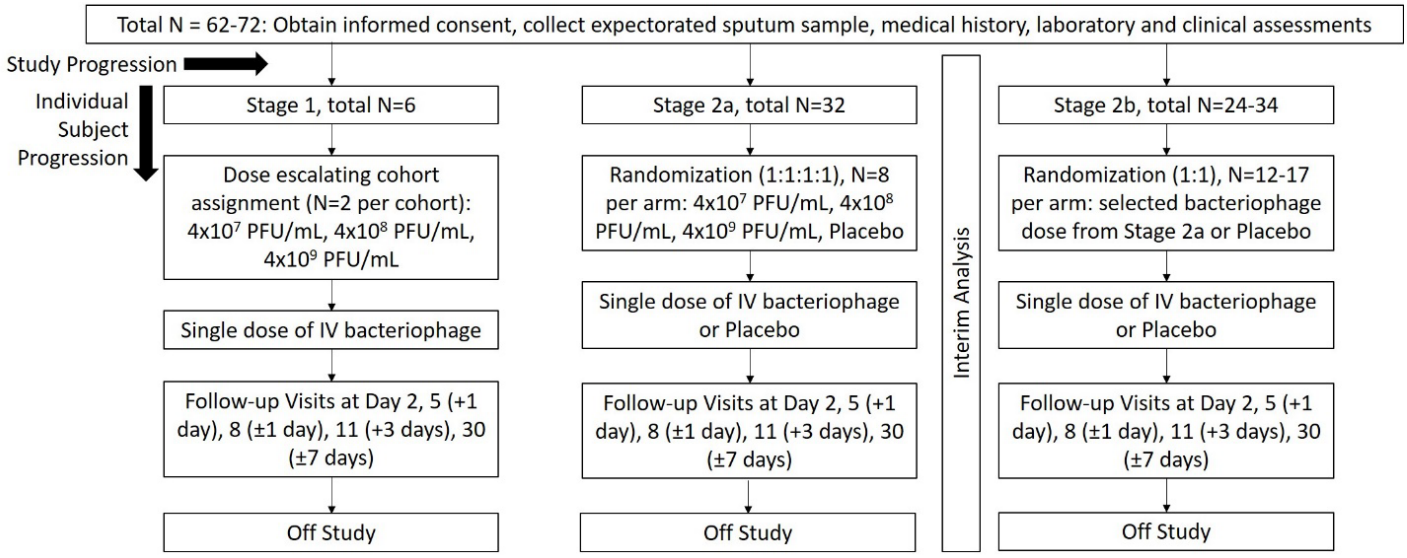
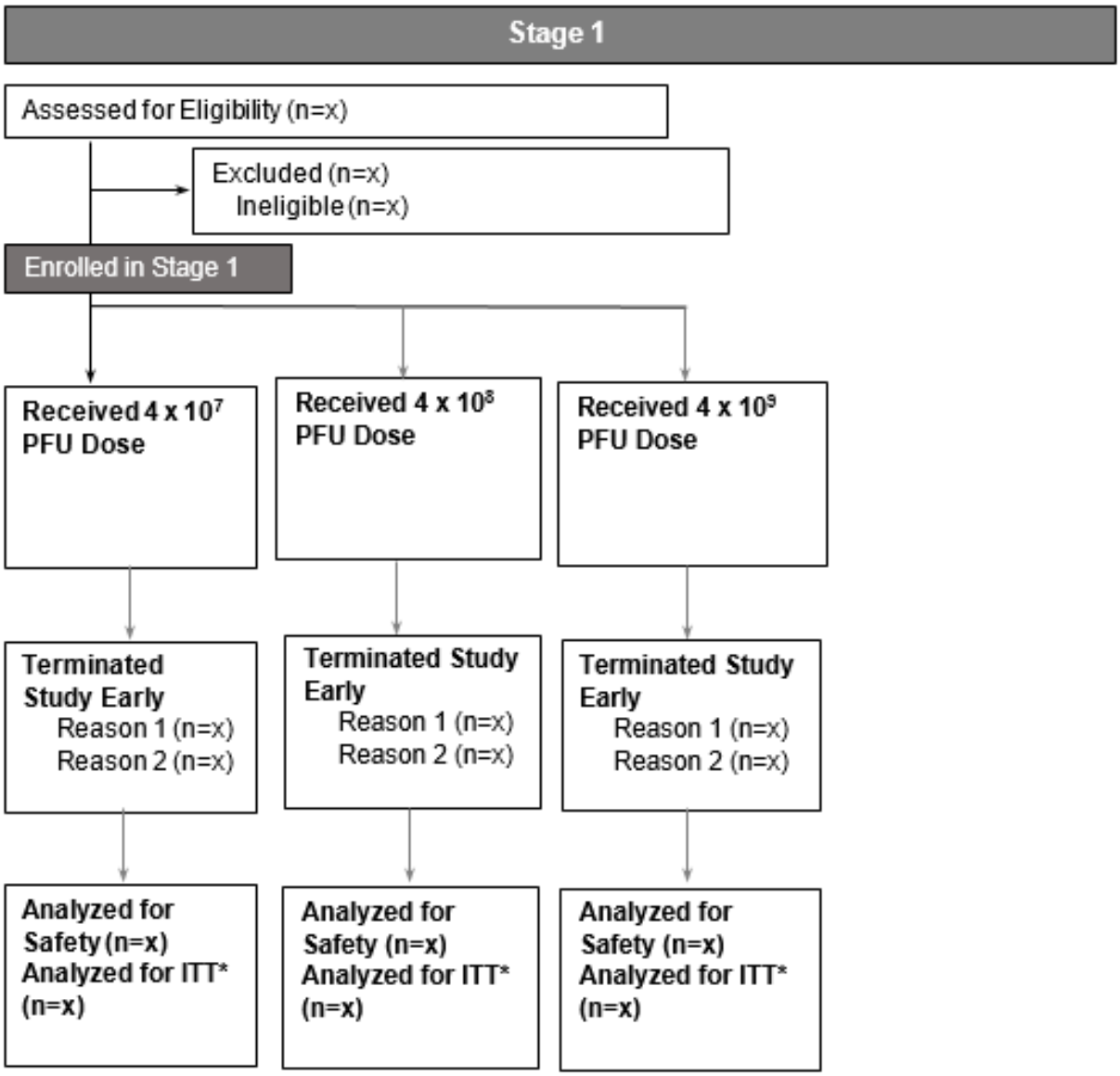


Figure 2: Study Flow Diagram



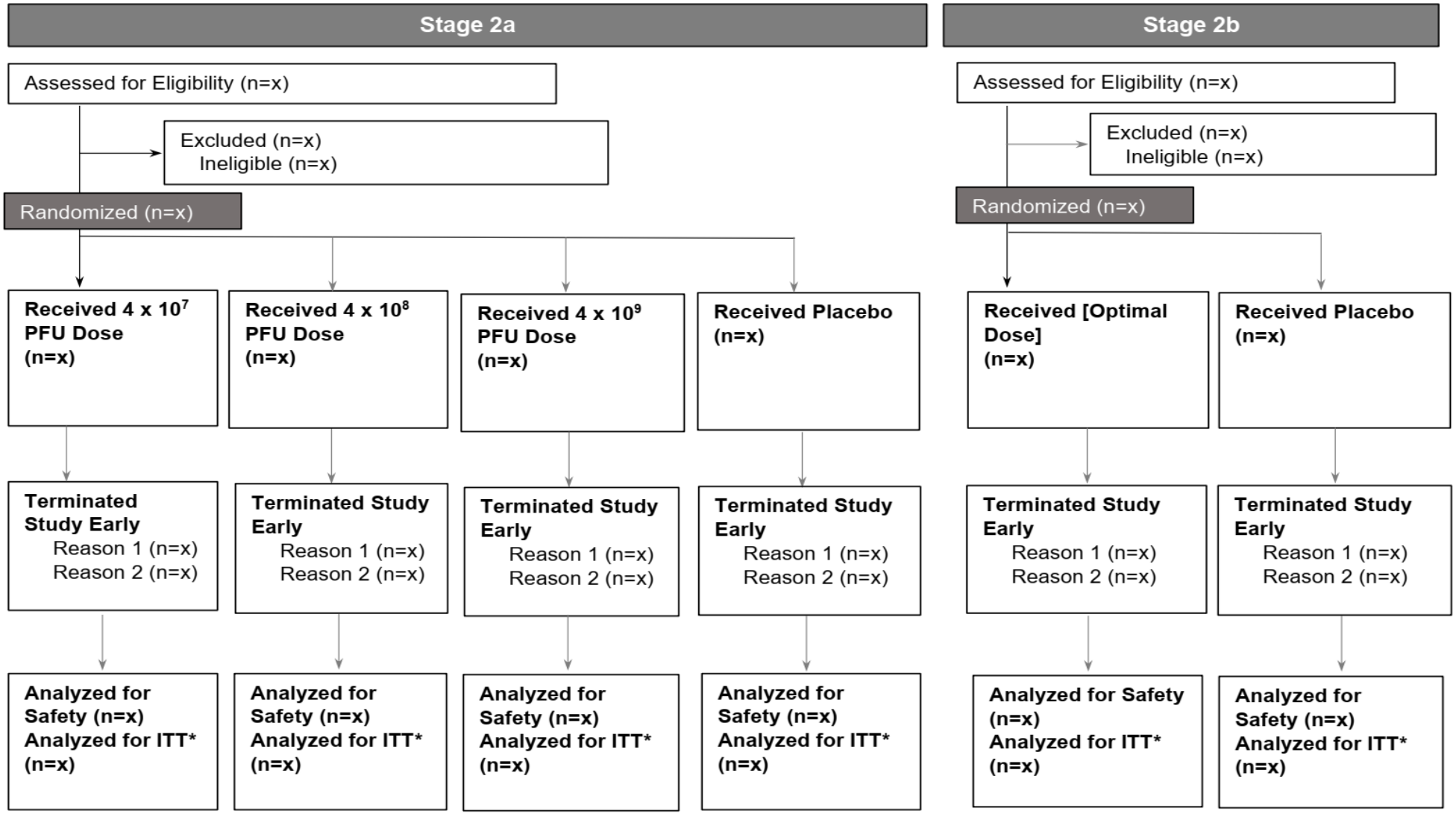
10.1 Disposition of Subjects

Figure 3: CONSORT Flow Diagram – Stage 1



** The ITT analysis population for Microbiological activity and DOOR endpoints will only contain subjects from Stage 2a and Stage 2b that received either the optimal dose of bacteriophage or placebo.*

Figure 4: CONSORT Flow Diagram – Stage 2a and 2b



** The ITT analysis population for Microbiological activity and DOOR endpoints will only contain subjects from Stage 2a and Stage 2b that received either the optimal dose of bacteriophage or placebo.*

14.2.2 Microbiological Activity/Benefit to Risk Profile Response Figures by Measure, Treatment/Vaccination, and Time Point

Figure 5: Median Colony Counts Over Time by Treatment Group – ITT Population, Stage 2a and 2b

[Implementation note: 'IV Bacteriophage' will be replaced with the Selected dose selected from the interim analysis.]

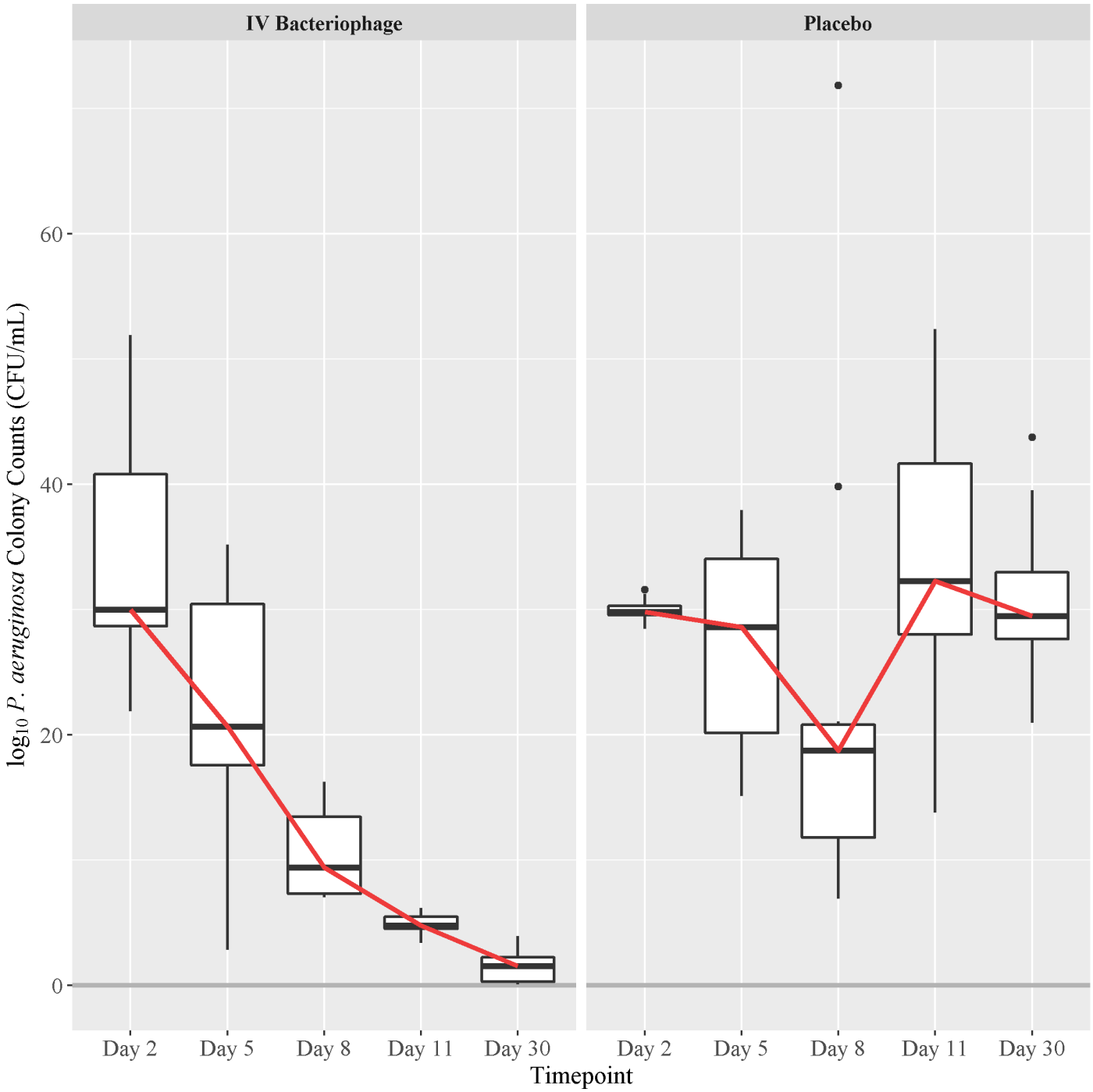
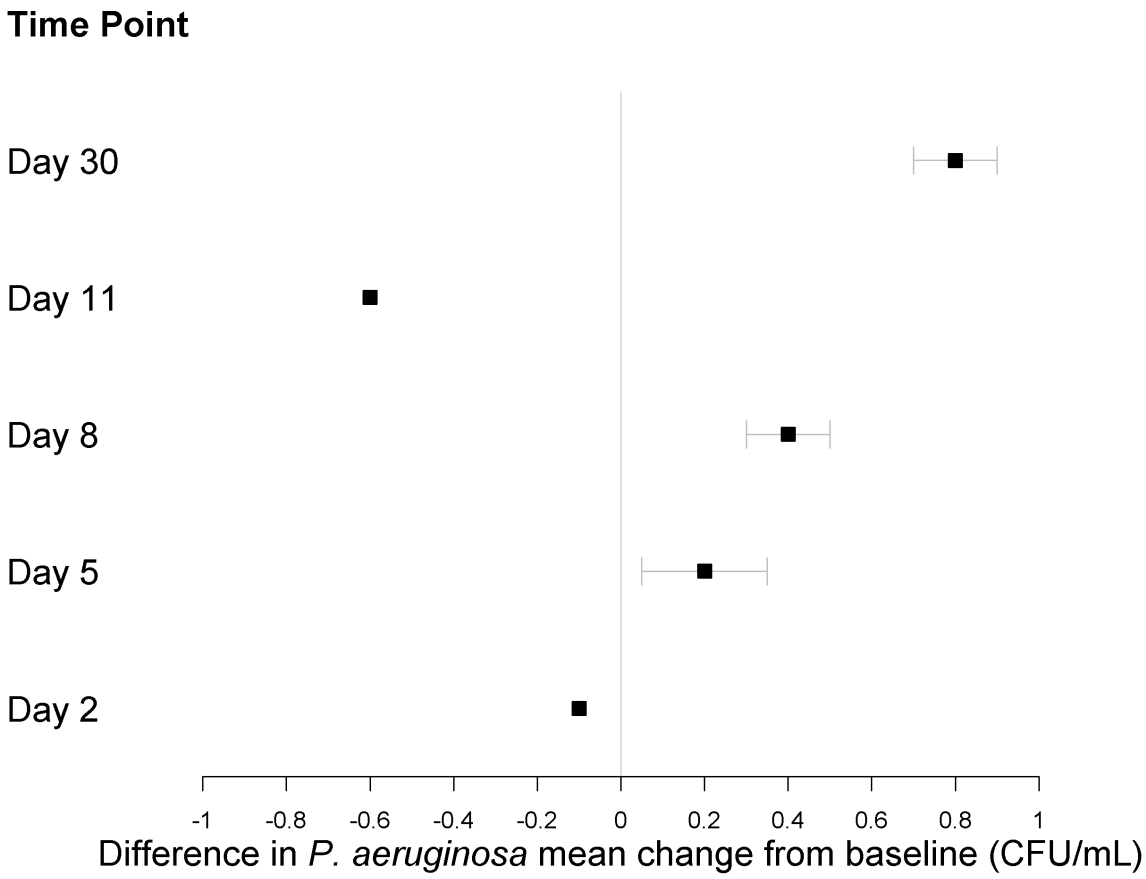


Figure 6: Forest Plot of Differences in *P. aeruginosa* Mean Change from Baseline By Time Point – ITT Population, Stage 2a and 2b



Figures with similar format:

Figure 7: Forest Plot of Differences in $\log_{10}$ *P. aeruginosa* Mean Change from Baseline by Time Point – ITT Population, Stage 2a and 2b

Figure 8: Forest Plot of Differences in *P. aeruginosa* Mean Change from Baseline by Time Point, Subgroup Analysis – ITT Population, Stage 2a and 2b

[Implementation note: This figure will repeat Figure 5 and will contain one panel for each subgroup: Susceptible – Yes, Susceptible – No, Co-infection – Yes, Co-infection – No.]

Figure 9: Forest Plot of Differences in log_{10} *P. aeruginosa* Mean Change from B Time, Subgroup Analysis – ITT Population

[Implementation note: This figure will repeat Figure 6 and will contain one panel for each subgroup: Susceptible – Yes, Susceptible – No, Co-infection – Yes, Co-infection – No.]

Figure 10: Forest Plot of Probabilities of DOOR Components at Day 8 – ITT Population

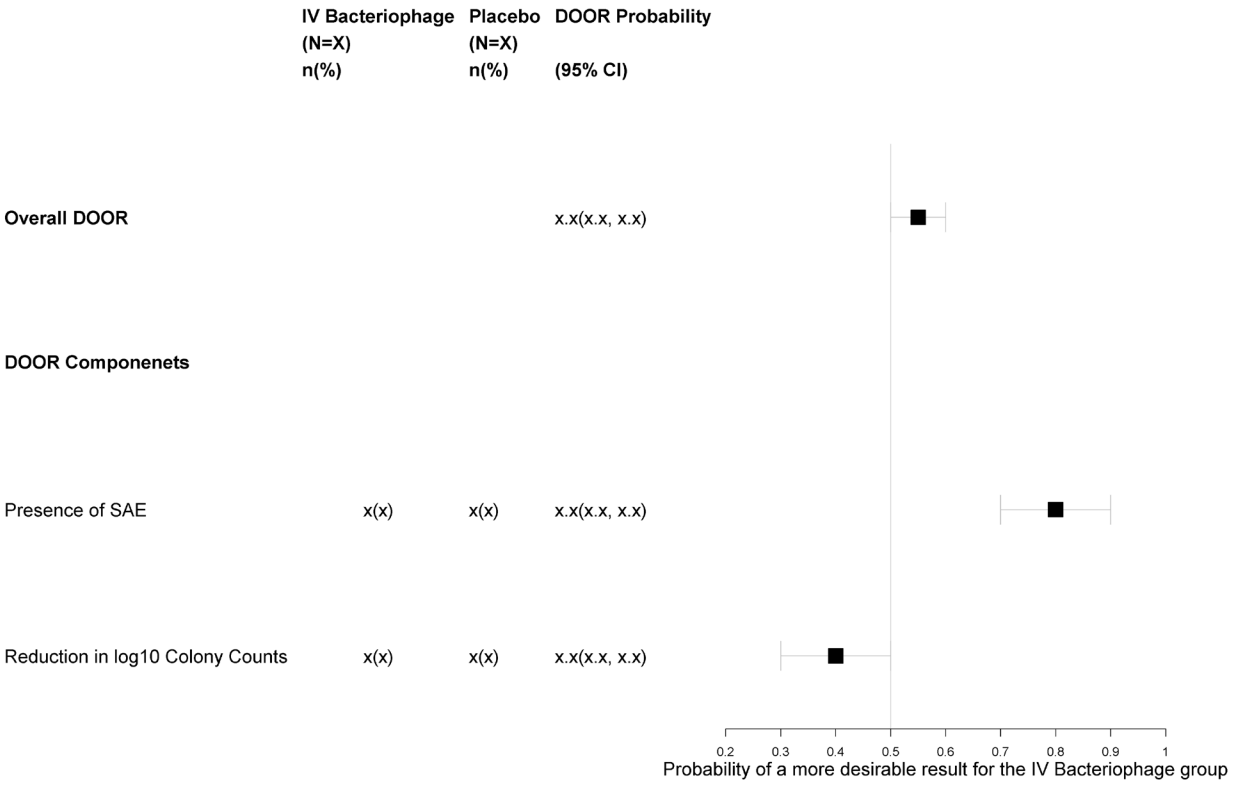


Figure 11: Forest Plot of DOOR Probability at Day 8, Subgroup Analysis – ITT Population

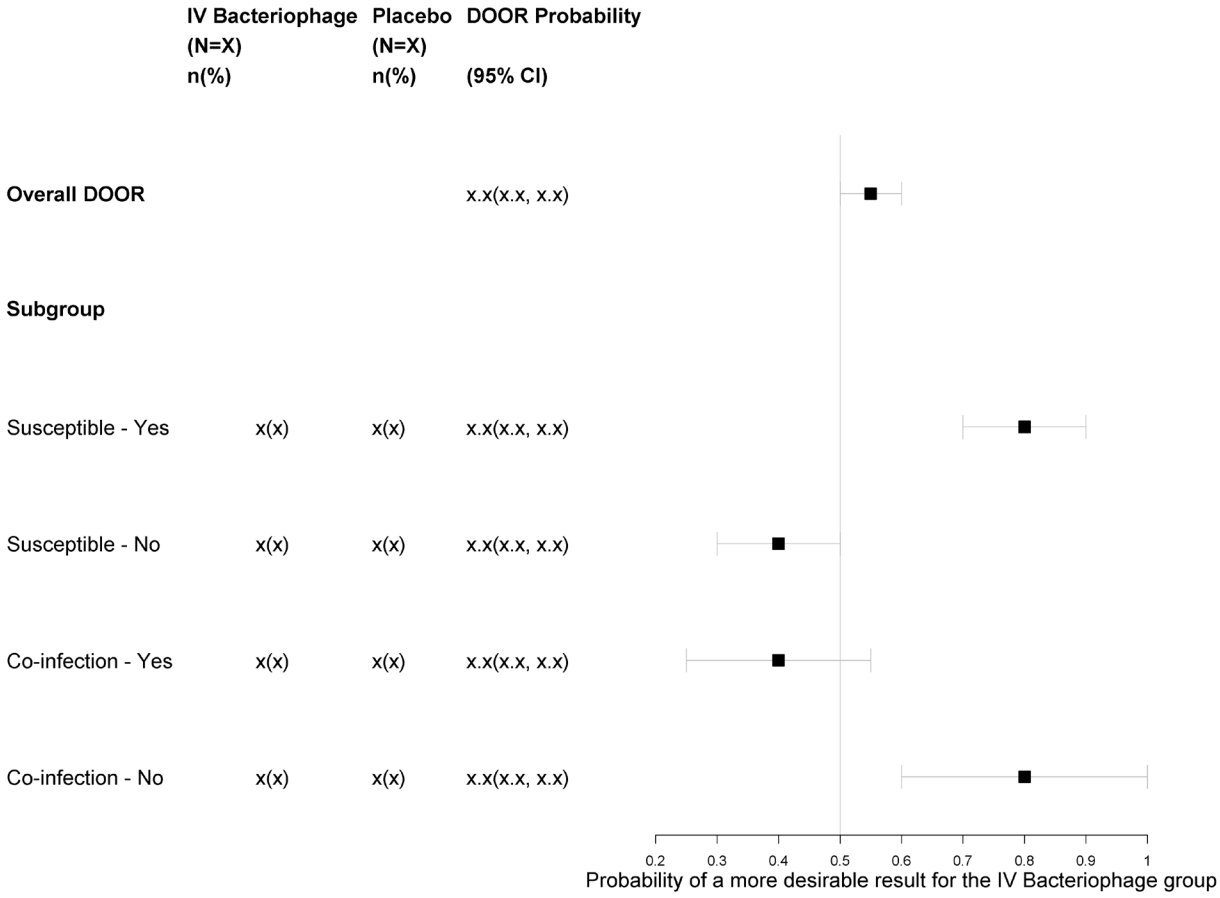


Figure 12: Forest Plot of Sequential Dichotomization of DOOR Categories with 95% CI

[Implementation note: This figure will have one panel for Day 2, Day 5, and Day 8.]

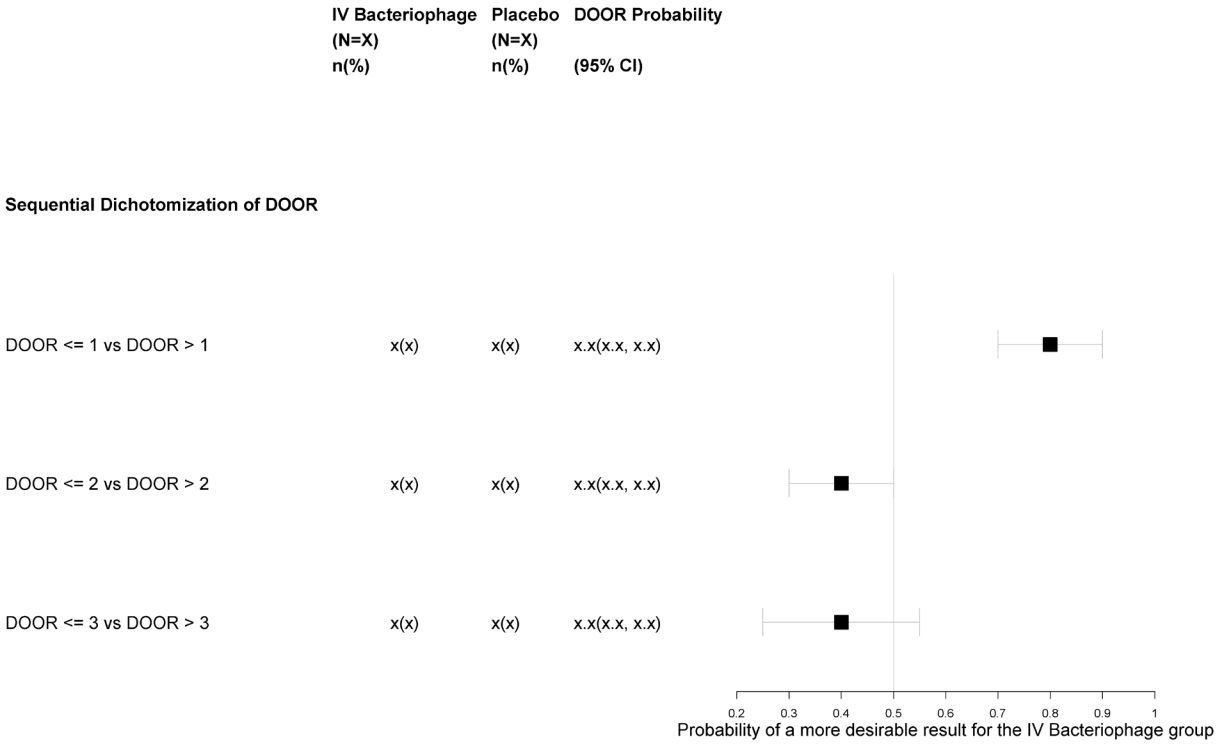
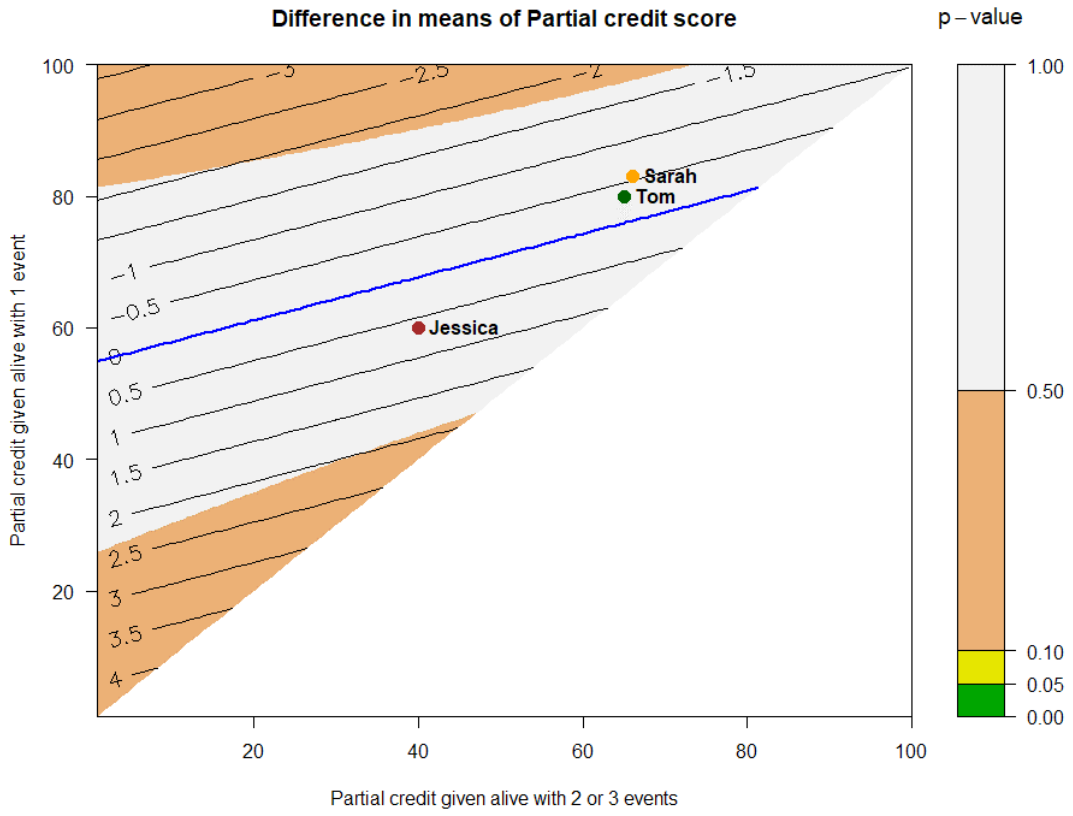


Figure 13: Difference in Means of Partial Credit Score by Time Point – ITT Population

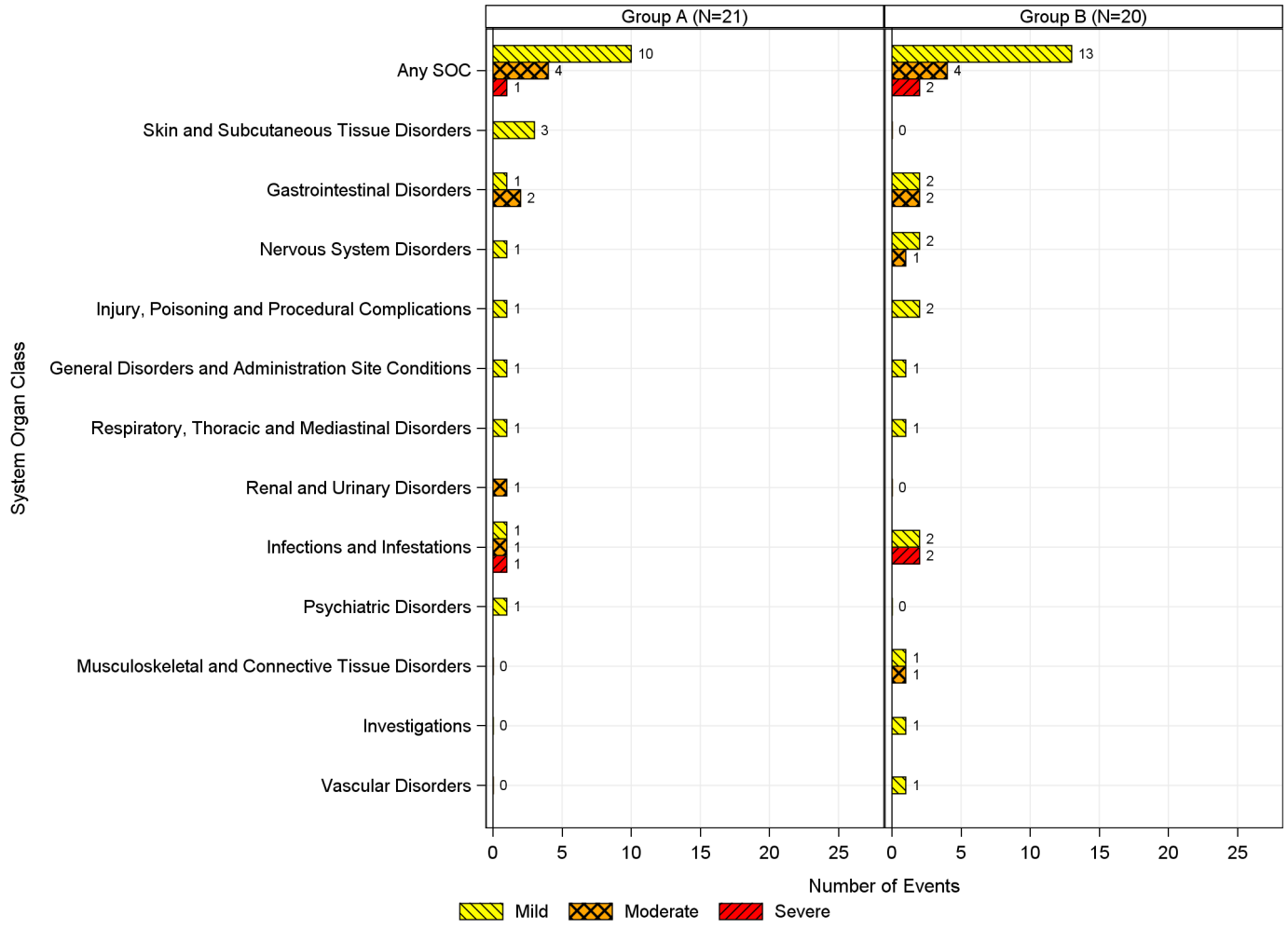
[Implementation note: Change x-axis label to "Partial credit given DOOR Rank 3" and change y-axis label to "Partial credit given DOOR Rank 2".]



14.3.1.2 Unsolicited Adverse Events

Figure 14: Frequency of Adverse Events by MedDRA System Organ Class, Severity, and Treatment Group, Stage 1

[Implementation Note: This figure will include panels for 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, and 4 x 10^9 PFU Dose. The SOCs should be sorted in descending frequency.]



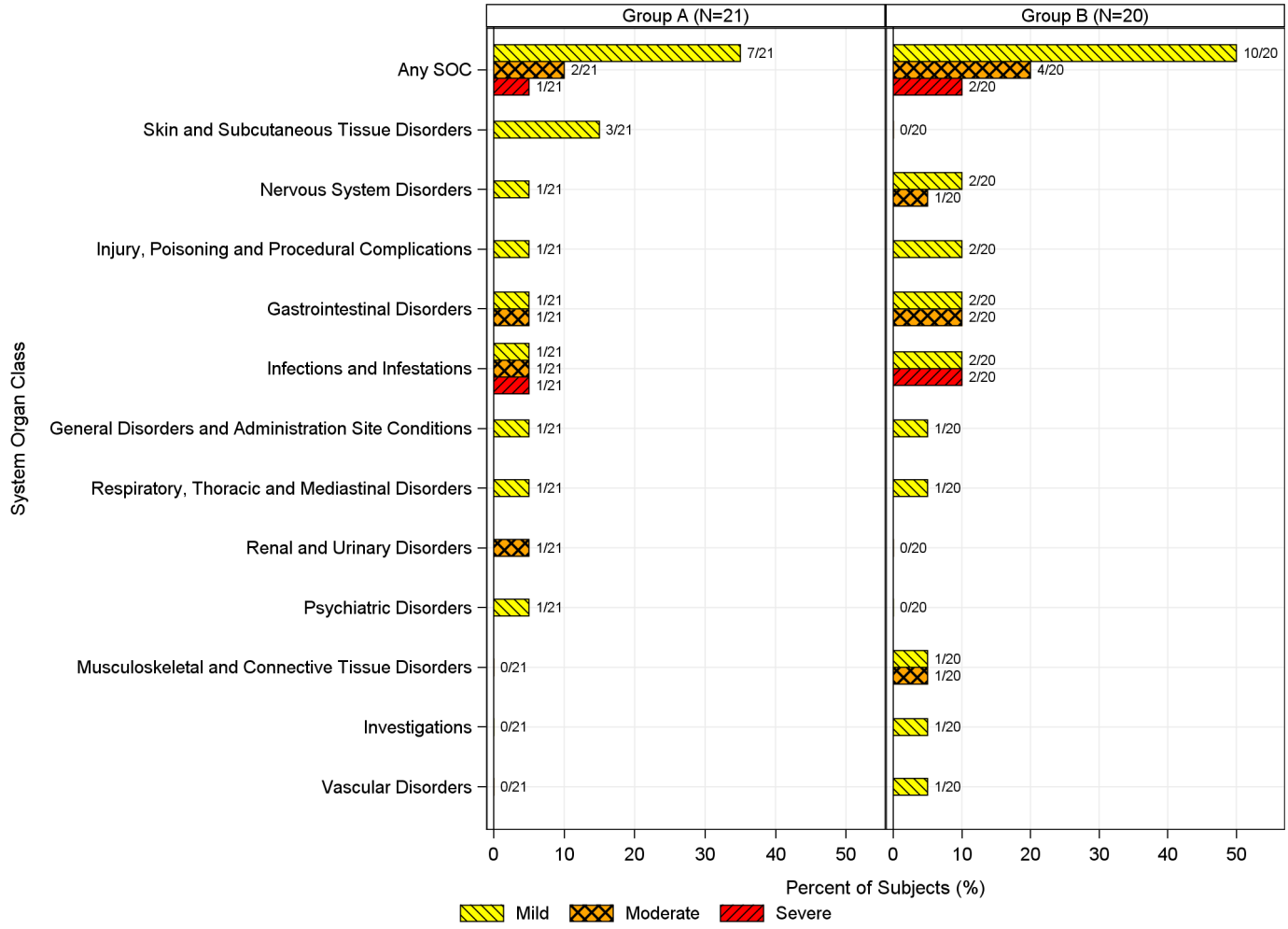
Figures with similar format:

Figure 15: Frequency of Adverse Events by MedDRA System Organ Class, Severity, and Treatment Group, Stage 2a

Figure 16: Frequency of Adverse Events by MedDRA System Organ Class, Severity, and Treatment Group, Stage 2a and 2b

Figure 17: Incidence of Adverse Events by MedDRA System Organ Class, Maximum Severity, and Treatment Group, Stage 1

[Implementation Note: This figure will include panels for 4 x 10^7 PFU Dose, 4 x 10^8 PFU Dose, and 4 x 10^9 PFU Dose. The SOCs should be sorted in descending frequency.]



Figures with similar format:

Figure 18: Incidence of Adverse Events by MedDRA System Organ Class, Maximum Severity, and Treatment Group, Stage 2a

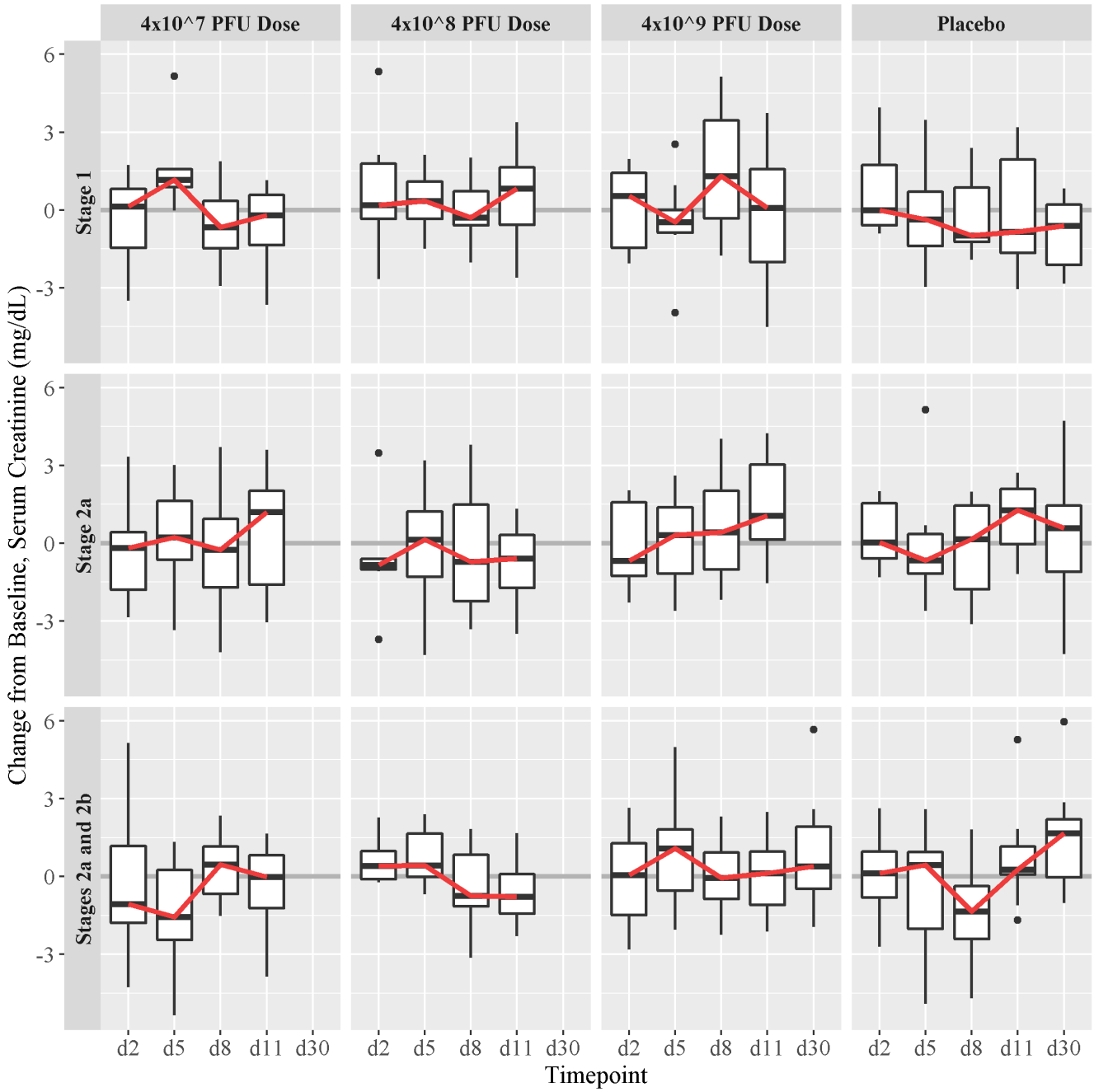
Figure 19: Incidence of Adverse Events by MedDRA System Organ Class, Maximum Severity, and Treatment Group, Stage 2a and 2b

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Figure 20: Chemistry Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Serum Creatinine

[Implementation note: Correct units will be displayed for each parameter. Titles will have 10^7, etc. displayed as superscript. 'd12' will be presented instead of 'd11' and only contain data from Stage 1 subjects.]



Figures with similar format:

Figure 21: Chemistry Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Blood Urea Nitrogen (BUN)

Figure 22: Chemistry Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Glucose

Figure 23: Chemistry Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Sodium

Figure 24: Chemistry Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Potassium

Figure 25: Chemistry Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Chloride

Figure 26: Chemistry Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Bicarbonate

Figure 27: Chemistry Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Calcium

14.3.5.2 Hematology Results

Figure 28: Hematology Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – RBC

This figure will repeat Figure 20 for RBC.

Figures with similar format:

Figure 29: Hematology Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Hemoglobin

Figure 30: Hematology Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Hematocrit

Figure 31: Hematology Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point– WBC

Figure 32: Hematology Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Platelets

Figure 33: Hematology Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Neutrophils

Figure 34: Hematology Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Lymphocytes

Figure 35: Hematology Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Monocytes

14.3.5.3 Liver Function Results

Figure 36: Liver Function Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Aspartate Aminotransferase

This figure will repeat Figure 20 for Aspartate Aminotransferase.

Figures with similar format:

Figure 37: Liver Function Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Alanine Aminotransferase

Figure 38: Liver Function Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Alkaline Phosphatase

Figure 39: Liver Function Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Total Bilirubin

Figure 40: Liver Function Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Albumin

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Figure 42: Liver Function Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Treatment Group, and Time Point – Total Protein

14.3.5.4 Displays of Vital Signs

Figure 43: Vital Signs Results by Scheduled Visits: Mean Changes from Baseline by Parameter, Treatment Group, and Time Point – Systolic Blood Pressure

This figure will repeat Figure 20 for Systolic Blood Pressure.

Figures with similar format:

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(Not included in SAP, but this is a placeholder for the CSR)

16.2 Database Listings by Subject

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Listing 2: 16.2.1: Early Terminations or Discontinued Subjects

[Implementation Note: Category will be either “Early Termination” or “Treatment Discontinuation”. In the “Reason” column, concatenate any “specify” fields, including AE number and DV number.

Sort order: Treatment Group, Subject ID, alphabetically by Category.]

Subject ID	Treatment Group	Category	Reason for Early Termination or Treatment Discontinuation	Study Day

16.2.2 Protocol Deviations

Listing 3: 16.2.2.1: Subject-Specific Protocol Deviations

[Implementation Note: In the "Deviation" column, concatenate any and all "specify" fields (including visit number, etc.). If "Reason for Deviation" is "Other", concatenate "specify" fields, separate by a colon, e.g., "Other: Subject refusal".

Sort order: Treatment Group, Subject ID, DV Number.]

Subject ID	Treatment Group	DV Number	Deviation	Deviation Category	Study Day	Reason for Deviation	Deviation Resulted in AE?	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Deviation Resolution	Comments

Listing 4: 16.2.2.2: Non-Subject-Specific Protocol Deviations

[Implementation Note: In the "Deviation" column, concatenate any and all "specify" fields (including visit number, etc.) If "Reason for Deviation" is "Other", concatenate "specify" fields, separated by a colon, e.g., "Other: Subject refusal".

Sort order: Treatment group, Subject ID, DV number.]

Site	Start Date	Deviation	End Date	Reason for Deviation	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Deviation Category	Deviation Resolution	Comments

16.2.3 Subjects Excluded from the Microbiological Activity/Benefit to Risk Profile Analysis

Listing 5: 16.2.3: Subjects Excluded from Analysis Populations

[Implementation Note: Sort order: Treatment group, Subject ID.]

Subject ID	Treatment Group	Analyses in which Subject is Included	Analyses from which Subject is Excluded	Results Available?	Reason Subject Excluded
		[e.g., Safety, ITT, PK]	[e.g., Safety, ITT, PK]		

Note: "Yes" in the "Results available" column indicates that available data were removed from the analysis. "No" indicates that no data were available for inclusion in the analysis.

16.2.4 Demographic Data

Listing 6: 16.2.4.1: Demographic Data

[Implementation Note: Sort order: Treatment group, Subject ID.]

Subject ID	Treatment Group	Sex	Age at Enrollment (years)	Ethnicity	Race	Weight at Screening (kg)	Height at Screening (cm)

Listing 7: 16.2.4.2: Pre-Existing and Concurrent Medical Conditions

[Implementation Note: Sort order: Treatment Group, Subject ID, MH number.]

Subject ID	Treatment Group	MH Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA System Organ Class	MedDRA High Level Term	MedDRA Preferred Term

16.2.5 Treatment Compliance Data

Listing 8: Product Administration Data

[Implementation Note: Listing should be sorted by Treatment Group and Subject ID.]

Subject ID	Treatment Group	Study Day	Symptoms Present at Baseline Assessment, if Any	Product Administration Site	Dose Start Time	Dose End Time	Product Completely Administered? If No, Volume Administered	Time of Post-Administration Assessment	Systemic Events Present	Local Events Present

Listing 9: Infusion Interruptions

[Implementation Note: Listing should be sorted by Treatment Group and Subject ID.]

Subject ID	Treatment Group	Study Day	Interruption Number	Infusion Halted Due to Drug-Related Hypersensitivity?	Infusion Interrupted Due to Non-Drug Safety Issues?	Infusion Interrupted Due to Infusion-Related Reaction?	Reason(s) Infusion Halted/Interrupted	Time Interrupted	Infusion Restarted?	Time Restarted

16.2.6 Individual Microbiological Activity/Benefit to Risk Profile Response Data

Listing 10: Listing of Colony Counts

[Implementation Note: Listing should be sorted by Treatment Group, Subject ID, and Planned Time Point. 'Other Organisms Recovered' field will concatenate the names of each organism recovered (if any) separated by a comma.]

Treatment Group	Subject ID	Planned Time Point	Other Organisms Recovered	Number of *P. aeruginosa* Morphotypes	Colony Count (CFU/mL)	Log_{10} Colony Count (CFU/mL)
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 2			xx	xx
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 5			xx	xx

Listing 11: *P. aeruginosa* Morphotype Results

[Implementation Note: Listing should be sorted by Treatment Group, Subject ID, Planned Time Point, and Medication. Rows will be repeated for each medication that minimum inhibitory concentration (MIC) testing is performed on, therefore there will be repeat data for all other columns.]

Treatment Group	Subject ID	Planned Time Point	Morphotype ID	Colony Size	Color	Mucoid Phenotype	Medication	MIC Results (mcg/mL)	Highest Number of Colonies
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 2			xx	xx	Colistin/polymyxin B		1.0×10^2 CFU/mL
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 2			xx	xx	Cefepime		1.0×10^2 CFU/mL

Listing 12: Individual DOOR Response Data

[Implementation Note: Listing should be sorted by Treatment Group, Subject ID, and Planned Time Point.]

Treatment Group	Subject ID	Planned Time Point	SAE Related to Study Product	Change in log_{10} Colony Counts from Baseline (CFU/mL)	DOOR Category
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 2	No	2	1
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 5	No	1	2

Listing 13: Phage Susceptibility Testing Results

[Implementation Note: Listing should be sorted by Treatment Group, Subject ID, and Planned Time Point.]

Treatment Group	Subject ID	Planned Time Point	Plaque Assay Result	Liquid Assay Result	Discordant Result	Phages Still Discordant After Repeat Testing
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 2	Susceptible/Not Susceptible	Susceptible/Not Susceptible	Y/N	PaWRA02Phi11
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 5				

Listing 14: Phage qPCR Results

[Implementation Note: Listing should be sorted by Treatment Group, Subject ID, and Planned Time Point.]

Treatment Group	Subject ID	Planned Time Point	Phage	Result
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 2	PaWRA02Phi11	1 x 10^6 PFU/mL
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 5		

Listing 15: Individual QoL Data – CFQ-R

[Implementation Note: Listing should be sorted by Treatment Group, Subject ID, Planned Time Point, and Domain.]

Treatment Group	Subject ID	Planned Time Point	Domain	QoL Score
$4x10^7$ IV Bacteriophage	BMB.XXXX	Baseline	Eat	
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 30	Eat	
$4x10^7$ IV Bacteriophage	BMB.XXXX	Baseline	Emotion	

Listing 16: Individual QoL Data – CFRSD

[Implementation Note: Listing should be sorted by Treatment Group, Subject ID, and Planned Time Point.]

Treatment Group	Subject ID	Planned Time Point	QoL Score
$4x10^7$ IV Bacteriophage	SST.XXXX	Baseline	
$4x10^7$ IV Bacteriophage	SST.XXXX	Day 2	
$4x10^7$ IV Bacteriophage	SST.XXXX	Day 5	

16.2.7 Adverse Events

Listing 17: 16.2.7.3: Unsolicited Adverse Events

[Implementation Note: If the event is ongoing (no stop date), indicate "ongoing" in the "Duration" column. In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. This listing includes all unsolicited adverse events. If there are no comments for an event, populate 'Comments' row with 'None'. Add columns for MedDRA HLT or lower level term (LLT) depending on halting criteria or other study needs.

Sort order: Treatment Group, Subject ID, Associated with Dose No., No. of Days Post Associated Dose. If the table will be multi-page, move the footnote/explanation to the footer so that it repeats for each page of the table.]

Adverse Event	Study Day of AE Onset	Duration (Days)	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA High Level Term	MedDRA Preferred Term
Treatment Group:, Subject ID:, AE Number:											
Comments:											
Treatment Group:, Subject ID:, AE Number:											
Comments:											

16.2.8 Individual Laboratory Measurements

Listing 18: 16.2.8.1: Clinical Laboratory Results – Chemistry

[Implementation note: Sort order: Treatment Group, Subject ID, and Planned Time Point.]

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range
								xx.xx – xx.xx

Listing 19: 16.2.8.2: Clinical Laboratory Results – Hematology

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range
								xx.xx – xx.xx

Listing 20: 16.2.8.3: Clinical Laboratory Results – Liver Function

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range
								xx.xx – xx.xx

16.2.9 Vital Signs and Physical Exam Findings

Listing 21: 16.2.9.1: Vital Signs

[Implementation note: Sort order: Treatment Group, Subject ID, and Planned Time Point.]

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Temperature (°C)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Heart Rate (BPM)	Respiratory Rate (breaths/min)	Weight (kg)	Height (cm)

Listing 22: 16.2.9.2: Physical Exam Findings

[Implementation note: Sort order: Treatment Group, Subject ID, and Planned Time Point.]

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Description; Number)

Listing 23: 16.2.9.3: Review of Systems Findings

[Implementation note: Sort order: Treatment Group, Subject ID, and Planned Time Point.]

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Body System	Abnormal Finding	Symptoms Exhibited	Reported as an AE? (AE Description; Number)

Listing 24: 16.2.9.2: Spirometry Measurements

[Implementation note: Sort order: Treatment Group, Subject ID, and Planned Time Point.]

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	FEV1 (Predicted FEV1)	FVC (Predicted FVC)	FEV1/FVC (Predicted FEV1/FVC)	FEF25-75% (Predicted FEF25-75%)

16.2.10 Concomitant Medications

Listing 25: 16.2.10: Prior Medications

[Implementation note: Sort order: Treatment group, Subject ID, concomitant medication number.]

Treatment Group	Subject ID	CM Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; Number)	Taken for a Condition on Medical History? (MH Description; Number)	ATC Level 1 (ATC Level 2)

Listing 26: 16.2.11: Concomitant Medications

[Implementation note: Sort order: Treatment group, Subject ID, concomitant medication number.]

Treatment Group	Subject ID	CM Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; Number)	Taken for a Condition on Medical History? (MH Description; Number)	ATC Level 1 (ATC Level 2)

16.2.11 Pregnancy Reports

Listing 27: 16.2.11.1: Pregnancy Reports – Maternal Information

[Implementation note: Sort order: Treatment group, Subject ID, pregnancy number.]

Treatment Group	Subject ID	Pregnancy Number	Study Day Corresponding to Estimated Date of Conception	Source of Maternal Information	Pregnancy Status	Mother's Pre-Pregnancy BMI	Mother's Weight Gain During Pregnancy	Tobacco, Alcohol, or Drug Use During Pregnancy?	Medications During Pregnancy?	Maternal Complications During Pregnancy?	Maternal Complications During Labor, Delivery, or Post-Partum?

Note: Maternal Complications are included in the Adverse Event listing. Medications taken during pregnancy are included in the Concomitant Medications Listing.

Listing 28: 16.2.11.2: Pregnancy Reports – Gravida and Para

			Live Births												
Subject ID	Pregnancy Number	Gravida	Extremely PB[a]	Very Early PB[a]	Early PB[a]	Late PB[a]	Early TB[a]	Full TB[b]	Late TB[b]	Post TB[b]	Still Births	Spontaneous Abortion/ Miscarriage	Elective Abortions	Therapeutic Abortions	Major Congenital Anomaly with Previous Pregnancy?

Note: Gravida includes the current pregnancy, para events do not.
[a] Preterm Birth
[b] Term Birth

Listing 29: 16.2.11.3: Pregnancy Reports – Live Birth Outcomes

Subject ID	Pregnancy Number	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Live Birth	Size for Gestational Age	Apgar Score, 1 minute	Apgar Score, 5 minutes	Cord pH	Congenital Anomalies?	Illnesses/ Hospitalizations within 1 Month of Birth?

Note: Congenital Anomalies are included in the Adverse Event listing.

Listing 30: 16.2.11.4: Pregnancy Reports – Still Birth Outcomes

Subject ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Still Birth	Size for Gestational Age	Cord pH	Congenital Anomalies?	Autopsy Performed?	If Autopsy, Etiology for Still Birth Identified?

Listing 31: 16.2.11.5: Pregnancy Reports – Spontaneous, Elective, or Therapeutic Abortion Outcomes

Subject ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Gestational Age at Termination	Abnormality in Product of Conception?	Reason for Therapeutic Abortion

CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN ADDENDUM
for
DMID Protocol: 20-0001
Study Title:

A Phase 1b/2, Multi-Centered, Randomized, Double-Blind, Placebo-Controlled Trial of the Safety and Microbiological Activity of a Single Dose of Bacteriophage Therapy in Cystic Fibrosis Subjects Colonized with *Pseudomonas aeruginosa*

NCT05453578

Version 1.0

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RESTRICTED

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LIST OF ABBREVIATIONS

CFU	Colony Forming Units
DOOR	Desirability of Outcome Ranking
LOD	Limit of Detection
PAG	Phage Advisory Group
SAP	Statistical Analysis Plan
TFL	Table, Figure, or Listing

1. INTRODUCTION

After an interim analysis the optimal dose for Stage 2b was selected on 02FEB2024. The decision was unanimous among Phage Advisory Group (PAG) members and was made based on the benefit to risk profile that considered both the safety profile of bacteriophage preparations as well as the observed reductions in *P. aeruginosa* colony forming units (CFU)/mL. During review of the interim data the issue of several subjects having undetectable *P. aeruginosa* colony counts came to light, where the lower detection limit was 10^4 CFU/mL per colony morphology for Stage 2a. Due to the data collection practices prior to the interim analysis, if *P. aeruginosa* was not recovered in a sputum sample with MALDI TOF confirmation of genus/species then null results were entered for the colony counts. As there was no detectable result (i.e. missing in the dataset) entered for the colony counts for these samples, they were treated as missing during data analysis.

This detection limit issue was unexpected at the time of planning, and the statistical analysis plan (SAP, version 1.0, dated 14NOV2023) does not address how to handle data censored due to the limit of detection. Under this scenario the exact value of an observation is unknown but is known to be below the lower limit of detection. Of the 32 subjects in the interim analysis, 3 had undetectable *P. aeruginosa* colony counts at baseline and 2 had undetectable *P. aeruginosa* colony counts at every time point post-baseline. As they were treated as missing for the interim analysis, a change from baseline was not calculable for these 5 subjects and they did not contribute information to the two primary analyses, i.e., change from baseline and the Desirability of Outcome Ranking (DOOR). These subjects were still analyzed for safety outcomes that factored into the dose selection decision.

This document describes the planned analyses as related to undetectable results. Because an undetectable result may or may not be a valid result (i.e. the sample did not contain sputum), both an analysis employing imputation and a sensitivity analysis will be considered where undetectable is treated as missing to both match the assumption that was used during the interim analysis and to explore the robustness of the assumption that all undetectable results are valid.

The primary analysis of the DOOR and *P. aeruginosa* colony count endpoints will substitute undetectable results using the lower limit of detection of the assay at the time of data collection. A sensitivity analysis will also be conducted wherein any undetectable values are treated as missing.

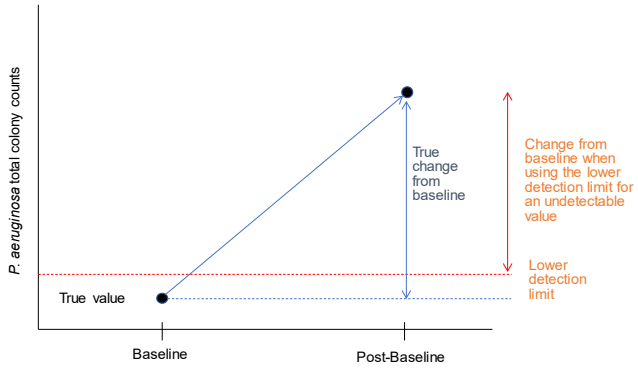
The tables, figures, and listings (TFLs) from v1.0 of the SAP that are affected by the change in assumptions of the primary analysis are listed in Appendices 1-3. The tables and figures in Appendix 1 and 2 will be repeated for the sensitivity analysis with the addition of ", Sensitivity Analysis" appended to the end of the TFL titles. Additionally, figures starting with Figure 19 and continuing through Figure 24 will be added to the report to visualize colony counts over time from Baseline through Day 8. The affected listings in Appendix 3 will not be repeated for the sensitivity analysis results but instead include either an implementation note to mark any substituted colony count (Listing 1) or a new column for 'Sensitivity Analysis DOOR Category' (Listing 2).

2. ANALYSIS CONSIDERING DETECTION STATUS

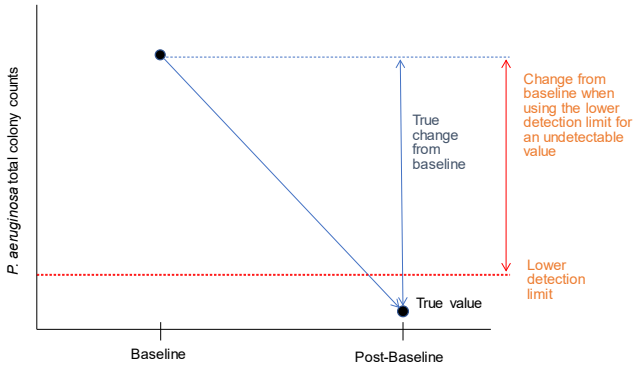
2.1. Substitution with the Lower Limit of Detection (LOD)

Undetectable *P. aeruginosa* total colony counts are substituted as 10^4 CFU/mL for Stage 2a and Stage 2b.

Although imputation of results below the lower limit of detection may result in biased estimates, it is a practical strategy to aid in analysis. As illustrated in the figures (A and B) below, this approach underestimates the change from baseline; if both baseline and post baseline are undetectable (this situation was not observed in Stage 2a), this approach also underestimates the change.



A. Baseline value is undetectable



B. Post-baseline value is undetectable

After the imputation, both the change from baseline and the DOOR outcome are derived and analyzed by the planned methods described in the SAP.

To evaluate the robustness of the results, a sensitivity analysis will be performed where all undetectable results are treated as missing. A tipping point analysis will be performed where differing percentages of undetectable results in the IV Bacteriophage and Placebo groups are substituted as 10^4. This analysis will help to determine a threshold where the proportion of samples that are assumed to be poor quality (treated as missing) begins to impact the primary DOOR outcome. This proportion can help inform conclusions about the robustness of the primary endpoint where all undetectable samples are treated as the limit of quantitation.

The tipping point analysis is shown in Table 30 and will replace the tipping point analysis in the main SAP v1.0 (Table 27). The tipping point will also be visualized in Figure 25.

2.2. *P. aeruginosa* Colony Count Detectability Status

The colony count detectability status is summarized over time, based on whether *P. aeruginosa* total colony counts are detectable, undetectable, or missing. This status is summarized descriptively with frequency and proportion by group, separately by stage 2a and 2b in Table 13 in this document. This will replace Table 25 from the main SAP v1.0 document.

3. LISTING OF TABLES, FIGURES, AND LISTINGS

Table, figure, and listing shells are presented in Appendices 1, 2, and 3.

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14.2 Microbiological Activity and Benefit to Risk Profile Data

Table 1: Change from Baseline in *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures by Treatment Group – ITT Population, Stage 2a and 2b

[Implementation notes: 'Selected Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	Treatment Group	Total Colony Counts						Change from Baseline						
		n	Mean	SD	Median	Q1, Q3[a]	Min, Max	n	Mean	SD	Median	Q1, Q3[a]	Min, Max	95% CI[b]
Baseline	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	-	-	-	-	-	-	-
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	-	-	-	-	-	-	-
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Maximum[c]	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Minimum[d]	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx

Notes: N=Number of subjects in the ITT Population in Stage 2a and 2b.
n=Number of subjects in the ITT Population with non-missing colony counts at the time point of interest. For the change from baseline, n represents the number of subjects in the ITT population with non-missing values at baseline and at the time point being assessed.
SD=Standard Deviation
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
Undetectable results are substituted as the LOD.
[a]Q1 and Q3 represent the 25th and 75th percentiles, respectively.
[b]95% CI (confidence interval) is calculated usinga t-distribution.
[c]Maximum is the maximum total colony counts and change from baseline for each subject over all time points.
[d]Minimum is the minimum total colony counts and change from baseline for each subject over all time points.

Table 2: Change from Baseline in *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures by Treatment Group – ITT Population, Stage 2a and 2b, Sensitivity Analysis

[Implementation notes: 'Selected Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	Treatment Group	Total Colony Counts						Change from Baseline						
		n	Mean	SD	Median	Q1, Q3[a]	Min, Max	n	Mean	SD	Median	Q1, Q3[a]	Min, Max	95% CI[b]
Baseline	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	-	-	-	-	-	-	-
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	-	-	-	-	-	-	-
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Maximum[c]	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Minimum[d]	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx

Notes: N=Number of subjects in the ITT Population in Stage 2a and 2b.
n=Number of subjects in the ITT Population with non-missing colony counts at the time point of interest. For the change from baseline, n represents the number of subjects in the ITT population with non-missing values at baseline and at the time point being assessed.
SD=Standard Deviation
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
Undetectable results are treated as missing.
[a]Q1 and Q3 represent the 25th and 75th percentiles, respectively.
[b]95% CI (confidence interval) is calculated from a t-distribution.
[c]Maximum is the maximum total colony counts and change from baseline for each subject over all time points.
[d]Minimum is the minimum total colony counts and change from baseline for each subject over all time points.

Table 3: Change from Baseline in log_{10} *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures by Treatment Group – ITT Population, Stage 2a and 2b

[Implementation notes: 'Selected Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	Treatment Group	log_{10} Total Colony Counts							Change from Baseline						
		n	Mean	SD	Median	Q1, Q3[a]	Min, Max	n	Mean	SD	Median	Q1, Q3[a]	Min, Max	95% CI[b]
Baseline	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	-	-	-	-	-	-	-
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	-	-	-	-	-	-	-
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Maximum[c]	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Minimum[d]	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx

Notes: N=Number of subjects in the ITT Population in Stage 2a and 2b.
n=Number of subjects in the ITT Population with non-missing colony counts at the time point of interest. For the change from baseline, n represents the number of subjects in the ITT population with non-missing values at baseline and at the time point being assessed.
SD=Standard Deviation
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
Undetectable results are substituted as the LOD.
[a]Q1 and Q3 represent the 25th and 75th percentiles, respectively.
[b]95% CI (confidence interval) is calculated using a t-distribution.
[c]Maximum is the maximum total colony counts and change from baseline for each subject over all time points.
[d]Minimum is the minimum total colony counts and change from baseline for each subject over all time points.

Table 4: Change from Baseline in log_{10} *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures by Treatment Group – ITT Population, Stage 2a and 2b, Sensitivity Analysis

[Implementation notes: 'Selected Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	Treatment Group	log_{10} Total Colony Counts							Change from Baseline						
		n	Mean	SD	Median	Q1, Q3[a]	Min, Max	n	Mean	SD	Median	Q1, Q3[a]	Min, Max	95% CI[b]
Baseline	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	-	-	-	-	-	-	-
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	-	-	-	-	-	-	-
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Maximum[c]	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
Minimum[d]	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x, xx.x	x.xx, x.xx

Notes: N=Number of subjects in the ITT Population in Stage 2a and 2b.
n=Number of subjects in the ITT Population with non-missing colony counts at the time point of interest. For the change from baseline, n represents the number of subjects in the ITT population with non-missing values at baseline and at the time point being assessed.
SD=Standard Deviation
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
Undetectable results are treated as missing.
[a]Q1 and Q3 represent the 25th and 75th percentiles, respectively.
[b]95% CI (confidence interval) is calculated using a t-distribution.
[c]Maximum is the maximum total colony counts and change from baseline for each subject over all time points.
[d]Minimum is the minimum total colony counts and change from baseline for each subject over all time points.

Table 5: Difference in Mean Change from Baseline in *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures – ITT Population, Stage 2a and 2b

[Implementation notes: The 95% CI for the difference in means is computed from Welch's t-test.]

Time Point	Difference in *P. aeruginosa* CFU/mL Mean Change from Baseline (95% CI[a])	Difference in $\log_{10}$ *P. aeruginosa* CFU/mL Mean Change from Baseline (95% CI[a])
Day 1 Post-infusion	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Day 2	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Day 5	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Day 8	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Day 30	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Maximum	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Minimum		
Any Day Post-infusion		

Notes: Difference calculated as Placebo – IV Bacteriophage.
Undetectable results are substituted as the LOD.
[a]The 95% CI for the difference in means is computed from Welch's t-test.

Table 6: Difference in Mean Change from Baseline in *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures – ITT Population, Stage 2a and 2b, Sensitivity Analysis

[Implementation notes: The 95% CI for the difference in means is computed from Welch's t-test.]

Time Point	Difference in *P. aeruginosa* CFU/mL Mean Change from Baseline (95% CI[a])	Difference in $\log_{10}$ *P. aeruginosa* CFU/mL Mean Change from Baseline (95% CI[a])
Day 1 Post-infusion	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Day 2	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Day 5	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Day 8	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Day 30	xx (xx.x, xx.x)	xx (xx.x, xx.x)
Maximum	xx (xx.x, xx.x)	xx (xx.x, xx.x)

Notes: Difference calculated as Placebo – IV Bacteriophage.
Undetectable results are treated as missing.
[a]The 95% CI for the difference in means is computed from Welch's t-test.

Table 7: Subgroup Analysis of Difference in Mean Change from Baseline in *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures – ITT Population, Stage 2a and 2b

[Implementation notes: The following subgroups will be included in this analysis: Susceptible to bacteriophages – Yes, Susceptible to bacteriophages – Yes, Presence of Co-infection with Organism X – Yes, Presence of Co-infection with Organism X – No. The 95% CI for the difference in means is computed usingWelch's t-test.]

Subgroup	Time Point	n_b (%)	n_p (%)	Difference in Mean Change from Baseline (95% CI[a])	Difference log_{10} in Mean Change from Baseline (95% CI[a])
Susceptible to Bacteriophages – Yes	Day 1 Post-infusion	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Day 2	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Day 5	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Day 8	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Day 30	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Maximum	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
…					
Presence of Co-infection with Organism X – No	Day 1 Post-infusion	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)

Notes: Difference calculated as Placebo – IV Bacteriophage. N_b=number of subjects in the ITT population who received IV bacteriophage within the subgroup category. N_p=number of subjects in the ITT population who received placebo within the subgroup category. Denominator for percentages is the total number of IV bacteriophage subjects in the ITT population for n_b and the total number of placebo subjects in the ITT population for n_p.
Undetectable results are substituted as the LOD.
[a] The 95% CI for the difference in means is computed using Welch's t-test.

Table 8: Subgroup Analysis of Difference in Mean Change from Baseline in *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures – ITT Population, Stage 2a and 2b, Sensitivity Analysis

[Implementation notes: The following subgroups will be included in this analysis: Susceptible to bacteriophages – Yes, Susceptible to bacteriophages – Yes, Presence of Co-infection with Organism X – Yes, Presence of Co-infection with Organism X – No. The 95% CI for the difference in means is computed using Welch's t-test.]

Subgroup	Time Point	n_b (%)	n_p (%)	Difference in Mean Change from Baseline (95% CI[a])	Difference log_{10} in Mean Change from Baseline (95% CI[a])
Susceptible to Bacteriophages – Yes	Day 1 Post-infusion	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Day 2	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Day 5	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Day 8	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Day 30	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
	Maximum	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)
…					
Presence of Co-infection with Organism X – No	Day 1 Post-infusion	x (x)	x (x)	xx (xx.x, xx.x)	xx (xx.x, xx.x)

Notes: Difference calculated as Placebo – IV Bacteriophage. N_b=number of subjects in the ITT population who received IV bacteriophage within the subgroup category. N_p=number of subjects in the ITT population who received placebo within the subgroup category. Denominator for percentages is the total number of IV bacteriophage subjects in the ITT population for n_b and the total number of placebo subjects in the ITT population for n_p.
Undetectable results are treated as missing.
[a] The 95% CI for the difference in means is computed using Welch's t-test.

Table 9: AUC of log_{10} *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures Over Time – ITT Population, Stage 2a and 2b

Time Point	Treatment Group	AUC				
		n	Mean	SD	Median	Min, Max
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Maximum	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x

Notes: N=Number of subjects in the ITT Population in Stage 2a and 2b.
n=Number of subjects in the ITT Population with non-missing colony counts at the time point of interest.
SD=Standard Deviation
AUC will be calculated using the linear trapezoidal rule as the area under the curve between baseline and the given time point.
Undetectable results are substituted as the LOD.

Table 10: AUC of log_{10} *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures Over Time – ITT Population, Stage 2a and 2b, Sensitivity Analysis

Time Point	Treatment Group	AUC				
		n	Mean	SD	Median	Min, Max
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
Maximum	Selected Dose (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo (N=X)	x	xx.x	xx.x	xx.x	xx.x, xx.x

Notes: N=Number of subjects in the ITT Population in Stage 2a and 2b.
n=Number of subjects in the ITT Population with non-missing colony counts at the time point of interest.
SD=Standard Deviation
AUC will be calculated using the linear trapezoidal rule as the area under the curve between baseline and the given time point.
Undetectable results are treated as missing.

Table 11: Difference in AUC of log_{10} *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures – ITT Population, Stage 2a and 2b

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis. The 95% CI for the difference in means is computed using Welch's t-test.]

Time Point	Treatment Group	Difference in AUC	95% CI[a]
Day 1 Post-infusion	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Day 2	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Day 5	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Day 8	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Day 30	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Maximum	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x

Notes: AUC will be calculated using the linear trapezoidal rule as the area under the curve between baseline and the given time point. Undetectable results are substituted as the LOD.
[a] The 95% CI for the difference in means is computed using Welch's t-test.

Table 12: Difference in AUC of log_{10} *P. aeruginosa* Total Colony Counts in Quantitative Sputum Cultures – ITT Population, Stage 2a and 2b, Sensitivity Analysis

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis. The 95% CI for the difference in means is computed using Welch's t-test.]

Time Point	Treatment Group	Difference in AUC	95% CI[a]
Day 1 Post-infusion	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Day 2	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Day 5	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Day 8	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Day 30	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x
Maximum	Selected IV Bacteriophage Dose (N=X)	xx	xx.x, xx.x

Notes: AUC will be calculated using the linear trapezoidal rule as the area under the curve between baseline and the given time point. Undetectable results are treated as missing.
[a] The 95% CI for the difference in means is computed using Welch's t-test.

Table 13: Percentage of Subjects with Detectable, Undetectable, and Missing DOOR Data by Time Point, Stage, and Treatment Group – ITT Population

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.

Time Point	Selected IV Bacteriophage Dose				Placebo				All Subjects			
	N	Detectable n (%)	Undetectable n (%)	Missing n (%)	N	Detectable n (%)	Undetectable n (%)	Missing n (%)	N	Detectable n (%)	Undetectable n (%)	Missing n (%)
Stage 2a												
Baseline	x	x	x	x	x	x	x	x	x	x	x	x
Day 1 Post-infusion	x	x	x	x	x	x	x	x	x	x	x	x
Day 2	x	x	x	x	x	x	x	x	x	x	x	x
Day 5	x	x	x	x	x	x	x	x	x	x	x	x
Day 8	x	x	x	x	x	x	x	x	x	x	x	x
Stage 2b												
…												

Notes: N=Number of subjects in the ITT population in each stage.
n=Number of subjects with missing data.

Table 14: DOOR Probability and 95% Confidence Interval by Day 8 – ITT Population, Stage 2a and 2b

Subjects With Non-missing DOOR – n (%)	Subjects With Missing DOOR – n (%)	DOOR Probability With IPW[a] (95% CI)[b]	DOOR Probability Without IPW[c] (95% CI)[b]
x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)

Notes: Undetectable results are substituted as the LOD.
[a]Probability of more desirable DOOR in IV bacteriophage + 0.5 (probability of equal DOOR) using the greatest reduction in *P. aeruginosa* CFU/mL by Day 8. This analysis uses IPW to handle the impact of missing values of DOOR.
[b]95% CI calculated using the method in Halperin et. al Superiority of IV bacteriophage vs. placebo is concluded if the lower bound of the 95% CI for the DOOR probability is above 0.5.
[c]This calculation does not use inverse probability weighting to handle missing DOOR values.

Table 15: DOOR Probability and 95% Confidence Interval by Day 8 – ITT Population, Stage 2a and 2b, Sensitivity Analysis

Subjects With Non-missing DOOR – n (%)	Subjects With Missing DOOR – n (%)	DOOR Probability With IPW[a] (95% CI)[b]	DOOR Probability Without IPW[c] (95% CI)[b]
x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)

Notes: Undetectable results are treated as missing.
[a]Probability of more desirable DOOR in IV bacteriophage + 0.5 (probability of equal DOOR) using the greatest reduction in *P. aeruginosa* CFU/mL by Day 8. This analysis uses IPW to handle the impact of missing values of DOOR.
[b]95% CI calculated using the method in Halperin et. al Superiority of IV bacteriophage vs. placebo is concluded if the lower bound of the 95% CI for the DOOR probability is above 0.5.
[c]This calculation does not use inverse probability weighting to handle missing DOOR values.

Table 16: Distribution of DOOR Categories by Treatment Group and Time Point – ITT Population, Stage 2a and 2b

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	DOOR Rank	Selected IV Bacteriophage Dose (N=X)		Placebo (N=X)	
		n	%	n	%
Day 1 Post-infusion	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Day 2	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Day 5	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Day 8	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	Xx
	Missing	x	xx	x	xx
Maximum[a]	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	Xx
	Any Rank	x	xx	x	xx

Notes: N=Number of subjects in the ITT Population in Stage 2a and 2b.
n=Number of subjects in the corresponding analysis population, treatment group, and DOOR rank
Undetectable results are substituted as the LOD.
[a]Maximum rows show DOOR ranks using greatest log_{10} reduction in *P. aeruginosa* CFU/mL by Day 8.

Table 17: Distribution of DOOR Categories by Treatment Group and Time Point – ITT Population, Stage 2a and 2b, Sensitivity Analysis

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	DOOR Rank	Selected IV Bacteriophage Dose (N=X)		Placebo (N=X)	
		n	%	n	%
Day 1 Post-infusion	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Day 2	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Day 5	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Day 8	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	Xx
	Missing	x	xx	x	xx
Maximum[a]	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	Xx
	Any Rank	x	xx	x	xx

Notes: N=Number of subjects in the ITT Population in Stage 2a and 2b.
n=Number of subjects in the corresponding analysis population, treatment group, and DOOR rank
Undetectable results are treated as missing.
[a]Maximum rows show DOOR ranks using greatest log_{10} reduction in *P. aeruginosa* CFU/mL by Day 8.

Table 18: Subgroup Analysis of DOOR at Day 8 – ITT Population, Stage 2a and 2b

[Implementation notes: 'Organism X' will be replaced with any organisms recovered on sputum cultures with one yes/no row for each organism.]

Subgroup	Subjects With Non-missing DOOR – n_b (%)	Subjects With Non-missing DOOR – n_p (%)	Subjects With Missing DOOR – n_b (%)	Subjects With Missing DOOR – n_p (%)	DOOR Probability With IPW[a] (95% CI)[b]	DOOR Probability Without IPW[c] (95% CI)[b]
Susceptible to Bacteriophages – Yes	x (x)	x (x)	x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Susceptible to Bacteriophages – No	x (x)	x (x)	x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Presence of Co-infection with Organism X – Yes	x (x)	x (x)	x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Presence of Co-infection with Organism X – No	x (x)	x (x)	x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)

Notes: n_b=number of subjects in the ITT population in Stage 2a and 2b who received IV bacteriophage within the subgroup category. n_p=number of subjects in the ITT population who received placebo within the subgroup category. Denominator for percentages is the total number of IV bacteriophage subjects in the ITT population for n_b and the total number of placebo subjects in the ITT population for n_p.

Undetectable results are substituted as the LOD.

[a]Probability of more desirable DOOR in IV bacteriophage arm + 0.5 (Probability of Equal DOOR) using the greatest reduction in *P. aeruginosa* CFU/mL by Day 8. This analysis uses IPW to handle the impact of missing values of DOOR.

[b]95% CI calculated using the method in Halperin et. al. Superiority of IV bacteriophage vs placebo is concluded if the lower bound of the 95% CI for the DOOR probability is above 0.5.

[c]This calculation does not use inverse probability weighting to handle missing DOOR values.

Table 19: Subgroup Analysis of DOOR at Day 8 – ITT Population, Stage 2a and 2b, Sensitivity Analysis

[Implementation notes: 'Organism X' will be replaced with any organisms recovered on sputum cultures with one yes/no row for each organism.]

Subgroup	Subjects With Non-missing DOOR – n_b (%)	Subjects With Non-missing DOOR – n_p (%)	Subjects With Missing DOOR – n_b (%)	Subjects With Missing DOOR – n_p (%)	DOOR Probability With IPW[a] (95% CI)[b]	DOOR Probability Without IPW[c] (95% CI)[b]
Susceptible to Bacteriophages – Yes	x (x)	x (x)	x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Susceptible to Bacteriophages – No	x (x)	x (x)	x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Presence of Co-infection with Organism X – Yes	x (x)	x (x)	x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Presence of Co-infection with Organism X – No	x (x)	x (x)	x (x)	x (x)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)

Notes: n_b=number of subjects in the ITT population in Stage 2a and 2b who received IV bacteriophage within the subgroup category. n_p=number of subjects in the ITT population who received placebo within the subgroup category. Denominator for percentages is the total number of IV bacteriophage subjects in the ITT population for n_b and the total number of placebo subjects in the ITT population for n_p.

Undetectable results are treated as missing.

[a]Probability of more desirable DOOR in IV bacteriophage arm + 0.5 (Probability of Equal DOOR) using the greatest reduction in *P. aeruginosa* CFU/mL by Day 8. This analysis uses IPW to handle the impact of missing values of DOOR.

[b]95% CI calculated using the method in Halperin et. al. Superiority of IV bacteriophage vs placebo is concluded if the lower bound of the 95% CI for the DOOR probability is above 0.5.

[c]This calculation does not use inverse probability weighting to handle missing DOOR values.

Table 20: Distribution of DOOR Categories by Subgroup, Treatment Group, and Time Point – ITT Population, Stage 2a and 2b

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis. For the sensitivity analysis the note "Undetectable results are substituted as the LOD" is replaced with "Undetectable results are treated as missing".]

Subgroup	DOOR Rank	Selected IV Bacteriophage Dose (N=X)		Placebo (N=X)	
		n	%	n	%
Day 1 Post-infusion					
Susceptible to Bacteriophages - Yes	Any Rank				
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Susceptible to Bacteriophages - No	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Presence of Co-infection with Organism X - Yes	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx

Table 20: Distribution of DOOR Categories by Subgroup, Treatment Group, and Time Point – ITT Population, Stage 2a and 2b *(continued)*

Subgroup	DOOR Rank	Selected IV Bacteriophage Dose (N=X)		Placebo (N=X)	
		n	%	n	%
Presence of Co-infection with Organism X - No	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Day 2					
…					
Day 5					
…		x	xx	x	xx
Day 8					
…		x	xx	x	Xx
Maximum[a]					
…					

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b in the given treatment group.
n=Number of subjects in the corresponding analysis population, treatment group, and DOOR rank.
Undetectable results are substituted as the LOD.
[a]Maximum rows show DOOR ranks using greatest log_{10} reduction in *P. aeruginosa* CFU/mL by Day 8.

Table 21: Distribution of DOOR Categories by Subgroup, Treatment Group, and Time Point – ITT Population, Stage 2a and 2b

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.]

Subgroup	DOOR Rank	Selected IV Bacteriophage Dose (N=X)		Placebo (N=X)	
		n	%	n	%
Day 1 Post-infusion					
Susceptible to Bacteriophages - Yes	Any Rank				
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Susceptible to Bacteriophages - No	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Presence of Co-infection with Organism X - Yes	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx

Table 21: Distribution of DOOR Categories by Subgroup, Treatment Group, and Time Point – ITT Population, Stage 2a and 2b *(continued)*

Subgroup	DOOR Rank	Selected IV Bacteriophage Dose (N=X)		Placebo (N=X)	
		n	%	n	%
Presence of Co-infection with Organism X - No	Any Rank	x	xx	x	xx
	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x	xx	x	xx
	Rank 4: SAE (related to study product)	x	xx	x	xx
	Missing	x	xx	x	xx
Day 2					
…					
Day 5					
…		x	xx	x	xx
Day 8					
…		x	xx	x	Xx
Maximum[a]					
…					

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b in the given treatment group.
n=Number of subjects in the corresponding analysis population, treatment group, and DOOR rank.
Undetectable results are treated as missing.
[a]Maximum rows show DOOR ranks using greatest log_{10} reduction in *P. aeruginosa* CFU/mL by Day 8.

Table 22: Cumulative Proportions of DOOR Categories – ITT Analysis Population, Stage 2a and 2b

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	DOOR Rank	Selected IV Bacteriophage Dose (N=X)			Placebo (N=X)	
		n (%)	Cumulative n (%)[a]	Cumulative Dichotomized Pr(DOOR)[a,b] (95% CI)[c]	n (%)	Cumulative n (%)[a]
Day 1 Post-infusion	Rank 1: No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	-	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-
Day 2	Rank 1: No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	-	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-
Day 5	Rank 1: No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-
Day 8	Rank 1: No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	-	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-

Table 22: Cumulative Proportions of DOOR Categories – ITT Analysis Population, Stage 2a and 2b *(continued)*

Time Point	DOOR Rank	Selected IV Bacteriophage Dose (N=X)			Placebo (N=X)	
		n (%)	Cumulative n (%)[a]	Cumulative Dichotomized Pr(DOOR)[a,b] (95% CI)[c]	n (%)	Cumulative n (%)[a]
Maximum[d]	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	-	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-

Notes: N=Number of subjects in the ITT Population in the given treatment group.
n=Number of subjects in the corresponding analysis population, treatment group, and DOOR rank
Undetectable results are substituted as the LOD.
[a]Cumulative n and percent do not include missing data.
[b]Probability of more desirable DOOR rank in IV Bacteriophage arm at each respective day + 0.5(Probability of Equal DOOR rank).
[c]95% CI calculated using the method in Halperin et. al.
[d]Maximum rows show DOOR ranks using greatest log_{10} reduction in *P. aeruginosa* CFU/mL by Day 8.

Table 23: Cumulative Proportions of DOOR Categories – ITT Analysis Population, Stage 2a and 2b, Sensitivity Analysis

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.]

		Selected IV Bacteriophage Dose (N=X)			Placebo (N=X)	
Time Point	**DOOR Rank**	**n (%)**	**Cumulative n (%)[a]**	**Cumulative Dichotomized Pr(DOOR)[a,b] (95% CI)[c]**	**n (%)**	**Cumulative n (%)[a]**
Day 1 Post-infusion	Rank 1: No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	-	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-
Day 2	Rank 1: No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	-	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-
Day 5	Rank 1: No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-
Day 8	Rank 1: No SAE (related to study product) and > 2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	-	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-

Table 23: Cumulative Proportions of DOOR Categories – ITT Analysis Population, Stage 2a and 2b, Sensitivity Analysis *(continued)*

Time Point	DOOR Rank	Selected IV Bacteriophage Dose (N=X)			Placebo (N=X)	
		n (%)	Cumulative n (%)[a]	Cumulative Dichotomized Pr(DOOR)[a,b] (95% CI)[c]	n (%)	Cumulative n (%)[a]
Maximum[d]	Rank 1: No SAE (related to study product) and > 2 log_{10} reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 2: No SAE (related to study product) and 1-2 log_{10} reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 3: No SAE (related to study product) and <1 log_{10} reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
	Rank 4: SAE (related to study product)	x (x)	x (x)	-	x (x)	x (x)
	Missing	x (x)	-	-	x (x)	-

Notes: N=Number of subjects in the ITT Population in the given treatment group.
n=Number of subjects in the corresponding analysis population, treatment group, and DOOR rank
Undetectable results are treated as missing.
[a]Cumulative n and percent do not include missing data.
[b]Probability of more desirable DOOR rank in IV Bacteriophage arm at each respective day + 0.5(Probability of Equal DOOR rank).
[c]95% CI calculated using the method in Halperin et. al.
[d]Maximum rows show DOOR ranks using greatest log_{10} reduction in *P. aeruginosa* CFU/mL by Day 8.

Table 24: Difference in Mean Partial Credit for DOOR Categories Through Day 8 – ITT Population, Stage 2a and 2b

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis. The 95% CI for the difference in means is computed Welch's t-test.]

Scenario	Time Point	Treatment Group	n	Mean (SD)	Difference in Means (95% CI)[a]
A: (1=100, 2=100, 3=100, 4=0)	Day 1 Post-infusion	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
	Day 2	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
	Day 5	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
	Day 8	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
	Maximum	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
[Extend the table to add Scenarios **B: (1=100, 2=100, 3=0, 4=0) and C: (1=100, 2=0, 3=0, 4=0)]**					

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b.
Undetectable results are substituted as the LOD.
n=Number of subjects in the corresponding analysis population with non-missing values of partial credit scores.
SD=Standard Deviation.
[a]The 95% CI for the difference in means is computed using Welch's t-test.

Table 25: Difference in Mean Partial Credit for DOOR Categories Through Day 8 – ITT Population, Stage 2a and 2b, Sensitivity Analysis

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis. The 95% CI for the difference in means is computed from Welch's t-test.]

Scenario	Time Point	Treatment Group	n	Mean (SD)	Difference in Means (95% CI)[a]
A: (1=100, 2=100, 3=100, 4=0)	Day 1 Post-infusion	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
	Day 2	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
	Day 5	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
	Day 8	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
	Maximum	Selected IV Bacteriophage Dose (N=X)	xx	xx (xx.x)	xx (xx.x, xx.x)
		Placebo (N=X)	xx	xx (xx.x)	
[Extend the table to add Scenarios **B: (1=100, 2=100, 3=0, 4=0) and C: (1=100, 2=0, 3=0, 4=0)]**					

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b.
Undetectable results are treated as missing.
n=Number of subjects in the corresponding analysis population with non-missing values of partial credit scores.
SD=Standard Deviation.
[a]The 95% CI for the difference in means is computed using Welch's t-test.

Table 26: Summary of DOOR Components Through Day 8 – ITT Analysis Population, Stage 2a and 2b

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.]

DOOR Component	Selected IV Bacteriophage Dose (N=X)			Placebo (N=X)	
	n (%)	Cumulative n (%)	Cumulative Dichotomized Pr(DOOR)[a] (95% CI)[b]	n (%)	Cumulative n (%)
Day 1 Post-infusion SAE					
No SAE (related to study product)	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
SAE	x (x)	x (x)	-	x (x)	x (x)
DOOR Probability for SAE Component[c]	x (100)	x (100)	x.x (x.x, x.x)	x (100)	x (100)
log10 Reduction in *P. aeruginosa* CFU/mL					
>2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
<1 $\log_{10}$ reduction/increase in *P. aeruginosa* CFU/mL	x (x)	x (x)	-	x (x)	x (x)
DOOR Probability for log10 Reduction in *P. aeruginosa* CFU/mL Component	x (100)	x (100)	x.x (x.x, x.x)	x (100)	x (100)
Day 2					
…					
Day 5					
…					
Day 8					
…					
Maximum[d]					
…					

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b with sputum collected at the given time point.
n=Number of subjects in the corresponding analysis population, treatment group, and DOOR category at the given time point.
Undetectable results are substituted as the LOD.
[a]Probability of more desirable DOOR component rank in IV Bacteriophage arm at each respective day + 0.5(Probability of Equal DOOR component rank). Dichotomized Pr(DOOR) of multiclass DOOR components classify the respective row class and more desirable classes (if any) as equally desirable.
[b]95% CI calculated using the method in Halperin et. al.
[c]Becasue the SAE Component is dichotomous, the DOOR Probability for that component and the Cumulative Dichotomized Pr(DOOR) should be equal.
[d]Maximum rows show DOOR ranks using greatest $\log_{10}$ reduction in *P. aeruginosa* CFU/mL by Day 8.

Table 27: Summary of DOOR Components Through Day 8 – ITT Analysis Population, Stage 2a and 2b

[Implementation notes: 'Selected IV Bacteriophage Dose' will be replaced with the dose chosen by the interim analysis.]

DOOR Component	Selected IV Bacteriophage Dose (N=X)			Placebo (N=X)	
	n (%)	Cumulative n (%)	Cumulative Dichotomized Pr(DOOR)[a] (95% CI)[b]	n (%)	Cumulative n (%)
Day 1 Post-infusion SAE					
No SAE (related to study product)	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
SAE	x (x)	x (x)	-	x (x)	x (x)
DOOR Probability for SAE Component[c]	x (100)	x (100)	x.x (x.x, x.x)	x (100)	x (100)
log10 Reduction in *P. aeruginosa* CFU/mL					
>2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
1-2 $\log_{10}$ reduction in *P. aeruginosa* CFU/mL	x (x)	x (x)	x.x (x.x, x.x)	x (x)	x (x)
<1 $\log_{10}$ reduction/increase in *P. aeruginosa* CFU/mL	x (x)	x (x)	-	x (x)	x (x)
DOOR Probability for log10 Reduction in *P. aeruginosa* CFU/mL Component	x (100)	x (100)	x.x (x.x, x.x)	x (100)	x (100)
Day 2					
…					
Day 5					
…					
Day 8					
…					
Maximum[d]					
…					

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b with sputum collected at the given time point.
n=Number of subjects in the corresponding analysis population, treatment group, and DOOR category at the given time point.
Undetectable results are treated as missing.
[a]Probability of more desirable DOOR component rank in IV Bacteriophage arm at each respective day + 0.5(Probability of Equal DOOR component rank). Dichotomized Pr(DOOR) of multiclass DOOR components classify the respective row class and more desirable classes (if any) as equally desirable.
[b]95% CI calculated using the method in Halperin et. al.
[c]Becasue the SAE Component is dichotomous, the DOOR Probability for that component and the Cumulative Dichotomized Pr(DOOR) should be equal.
[d]Maximum rows show DOOR ranks using greatest $\log_{10}$ reduction in *P. aeruginosa* CFU/mL by Day 8.

Table 28: Change in log_{10} *P. aeruginosa* Colony Counts by Treatment Group and Morphology – ITT Population, Stage 2a and 2b

[Implementation note: 'Selected Dose' will be replaced with the dose chosen by the interim analysis. For the sensitivity analysis the note "Undetectable results are substituted as the LOD" is replaced with "Undetectable results are treated as missing".]

Time Point	Treatment Group	Colony Counts						Change from Baseline						
		n	Mean	SD	Median	Q1, Q3[a]	Min, Max	n	Mean	SD	Median	Min, Max	Q1, Q3[a]	95% CI[b]
[Morphology 1]														
Baseline	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	-	-	-	-	-	-
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	-	-	-	-	-	-
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Maximum	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
[Repeat for all morphologies]														

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b.
n=Number of subjects in the ITT population in Stage 2a and 2b with non-missing colony counts at the time point of interest. For the change from baseline, n represents the number of subjects in the ITT population with non-missing values at baseline and at the time point being assessed.
SD=Standard Deviation
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
Undetectable results are substituted as the LOD.
[a]Q1 and Q3 represent the 25th and 75th percentiles, respectively.
[b]95%CI is calculated using a t-distribution.

Table 29: Change in log_{10} *P. aeruginosa* Colony Counts by Treatment Group and Morphology – ITT Population, Stage 2a and 2b, Sensitivity Analysis

[Implementation note: 'Selected Dose' will be replaced with the dose chosen by the interim analysis.]

Time Point	Treatment Group	Colony Counts						Change from Baseline						
		n	Mean	SD	Median	Q1, Q3[a]	Min, Max	n	Mean	SD	Median	Min, Max	Q1, Q3[a]	95% CI[b]
[Morphology 1]														
Baseline	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	-	-	-	-	-	-
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	-	-	-	-	-	-
Day 1 Post-infusion	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Day 2	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Day 5	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Day 8	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Day 30	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
Maximum	Selected Dose (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
	Placebo (N=X)	x	xx.x	xx.x	xx	xx, xx	xx, xx	x	xx.x	xx.x	xx	xx, xx	xx, xx	x.xx, x.xx
[Repeat for all morphologies]														

Notes: N=Number of subjects in the ITT population in Stage 2a and 2b.
n=Number of subjects in the ITT population in Stage 2a and 2b with non-missing colony counts at the time point of interest. For the change from baseline, n represents the number of subjects in the ITT population with non-missing values at baseline and at the time point being assessed.
SD=Standard Deviation
Baseline is defined as the last measurement taken prior to dosing on Study Day 1.
Undetectable results are treated as missing.
[a]Q1 and Q3 represent the 25th and 75th percentiles, respectively.
[b]95%CI is calculated using a t-distribution.

Table 30: Tipping Point Analysis – ITT Population, Stage 2a and 2b

	Substituted Colony Counts in IV Bacteriophage									
Substituted Colony Counts in Placebo	**10%**	**20%**	**30%**	**40%**	**50%**	**60%**	**70%**	**80%**	**90%**	**100%**
10%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
20%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
30%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
40%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
50%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
60%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
70%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
80%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
90%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
100%	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)

Note: Values shown are the DOOR probability, i.e., the probability of more desirable DOOR in IV bacteriophage arm + 0.5 (probability of equal DOOR) using the greatest reduction in *P. aeruginosa* CFU/mL by Day 8, and the associated 95% CI obtained through the method described in Halperin et. al.

APPENDIX 2. FIGURE MOCK-UPS

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14.2.2 Microbiological Activity/Benefit to Risk Profile Response Figures by Measure, Treatment/Vaccination, and Time Point

Figure 1: Median Colony Counts Over Time by Treatment Group – ITT Population, Stage 2a and 2b

[Implementation note: 'IV Bacteriophage' will be replaced with the Selected dose selected from the interim analysis.]

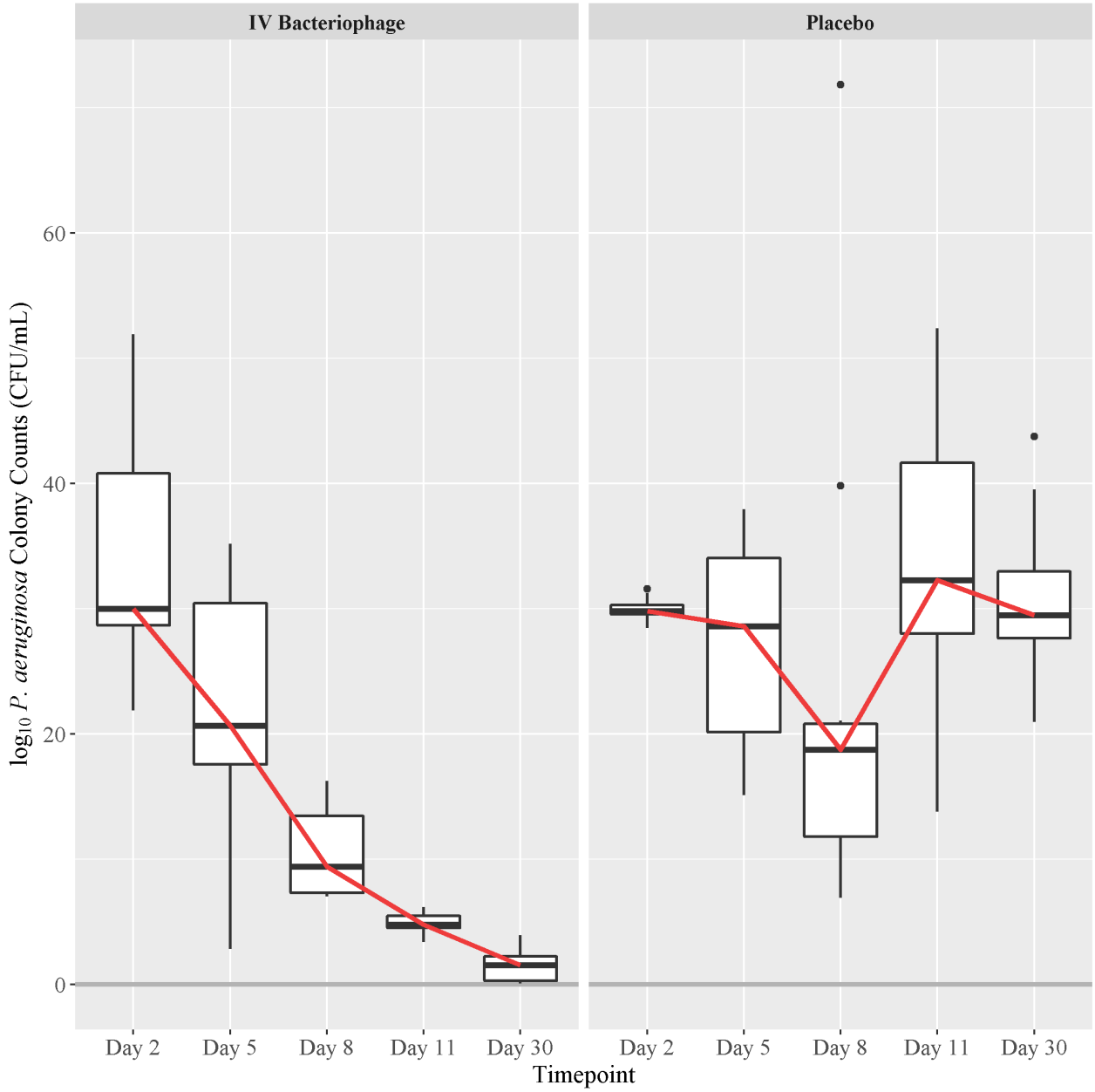
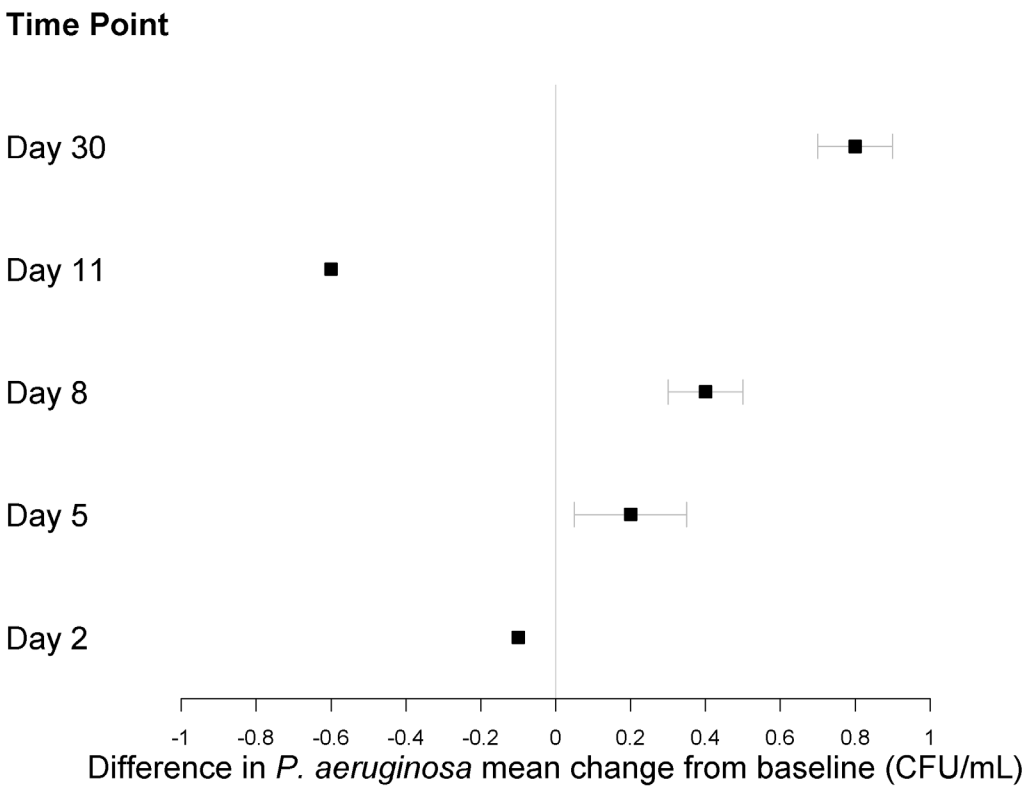


Figure with similar format:

Figure 2: Median Colony Counts Over Time by Treatment Group – ITT Population, Stage 2a and 2b, Sensitivity Analysis

Figure 3: Forest Plot of Differences in *P. aeruginosa* Mean Change from Baseline By Time Point – ITT Population, Stage 2a and 2b



Figures with similar format:

Figure 4: Forest Plot of Differences in *P. aeruginosa* Mean Change from Baseline By Time Point – ITT Population, Stage 2a and 2b, Sensitivity Analysis

Figure 5: Forest Plot of Differences in $\log_{10}$ *P. aeruginosa* Mean Change from Baseline by Time Point – ITT Population, Stage 2a and 2b

Figure 6: Forest Plot of Differences in $\log_{10}$ *P. aeruginosa* Mean Change from Baseline by Time Point – ITT Population, Stage 2a and 2b, Sensitivity Analysis

Figure 7: Forest Plot of Differences in *P. aeruginosa* Mean Change from Baseline by Time Point, Subgroup Analysis – ITT Population, Stage 2a and 2b

[Implementation note: This figure will repeat Figure 3 and will contain one panel for each subgroup: Susceptible – Yes, Susceptible – No, Co-infection – Yes, Co-infection – No.]

Figure 8: Forest Plot of Differences in *P. aeruginosa* Mean Change from Baseline by Time Point, Subgroup Analysis – ITT Population, Stage 2a and 2b, Sensitivity Analysis

[Implementation note: This figure will repeat Figure 3 and will contain one panel for each subgroup: Susceptible – Yes, Susceptible – No, Co-infection – Yes, Co-infection – No.]

Figures with similar format *(continued)*

Figure 9: Forest Plot of Differences in log_{10} *P. aeruginosa* Mean Change from B Time, Subgroup Analysis – ITT Population

[Implementation note: This figure will repeat Figure 3 and will contain one panel for each subgroup: Susceptible – Yes, Susceptible – No, Co-infection – Yes, Co-infection – No.]

Figure 10: Forest Plot of Differences in log_{10} *P. aeruginosa* Mean Change from B Time, Subgroup Analysis – ITT Population, Sensitivity Analysis

[Implementation note: This figure will repeat Figure 3 and will contain one panel for each subgroup: Susceptible – Yes, Susceptible – No, Co-infection – Yes, Co-infection – No.]

Figure 11: Forest Plot of Probabilities of DOOR Components at Day 8 – ITT Population

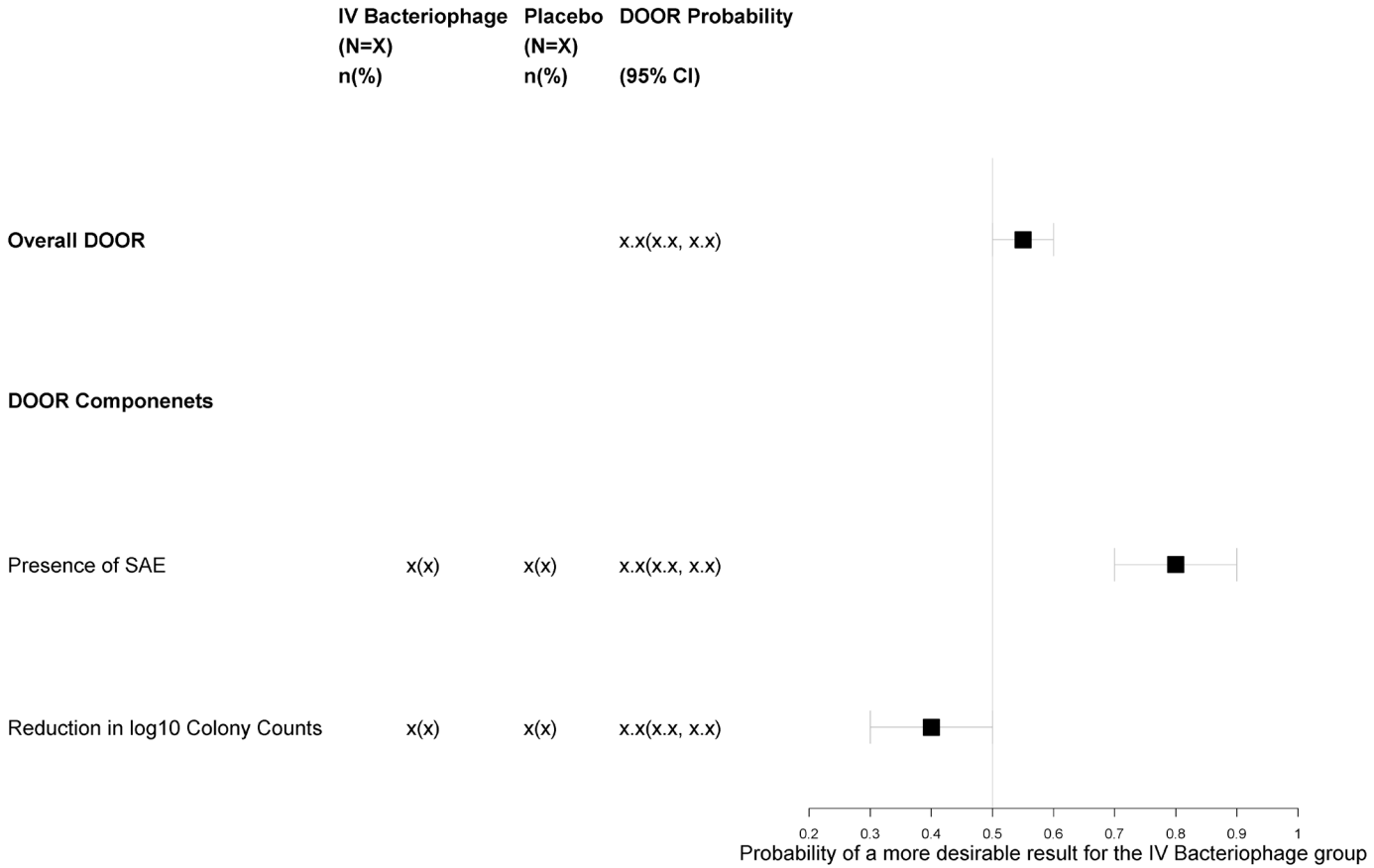


Figure with similar format:

Figure 12: Forest Plot of Probabilities of DOOR Components at Day 8 – ITT Population, Sensitivity Analysis

Figure 13: Forest Plot of DOOR Probability at Day 8, Subgroup Analysis – ITT Population

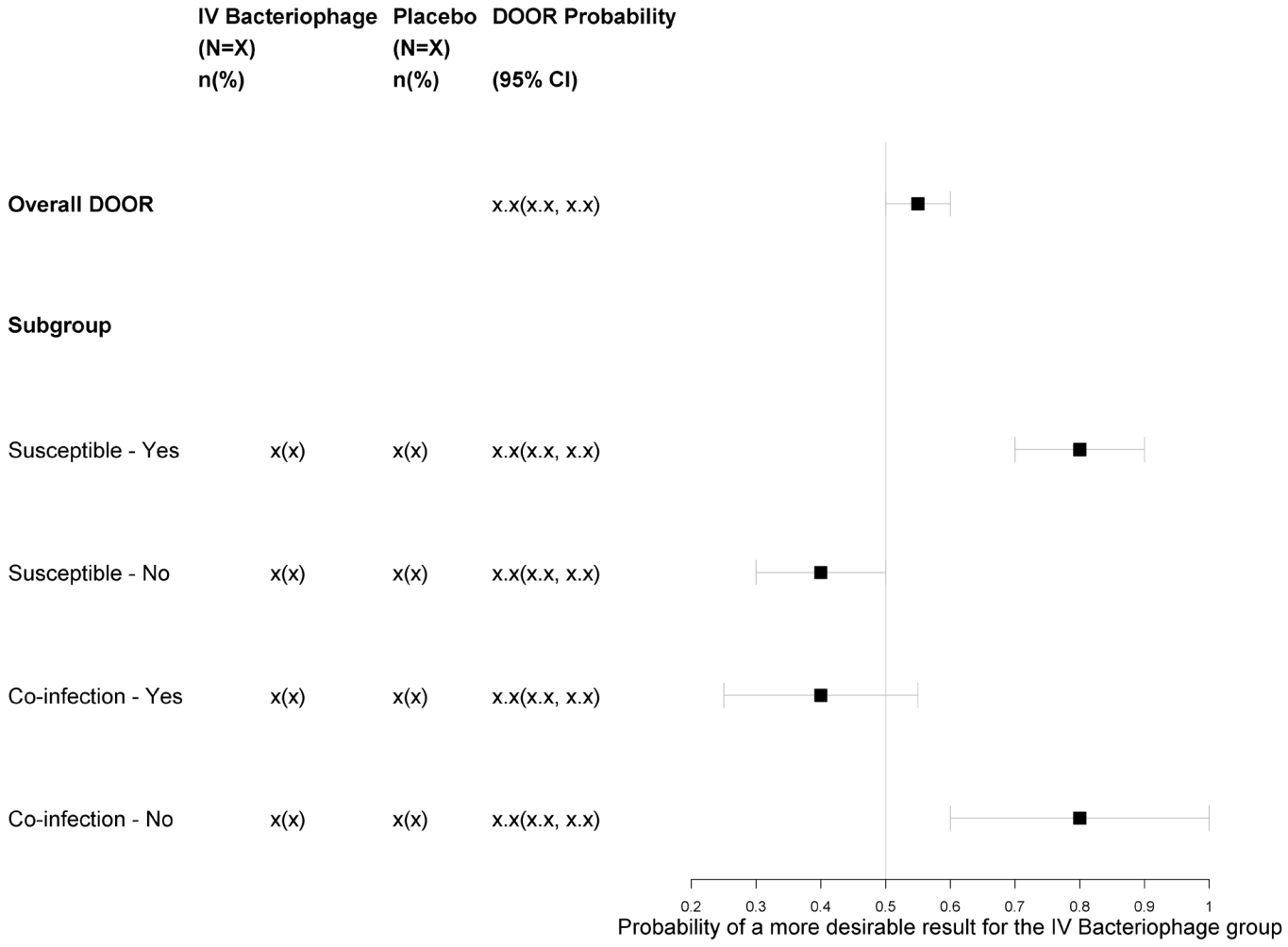


Figure with similar format:

Figure 14: Forest Plot of DOOR Probability at Day 8, Subgroup Analysis – ITT Population, Sensitivity Analysis

Figure 15: Forest Plot of Sequential Dichotomization of DOOR Categories with 95% CI

[Implementation note: This figure will have one panel for Day 2, Day 5, and Day 8.]

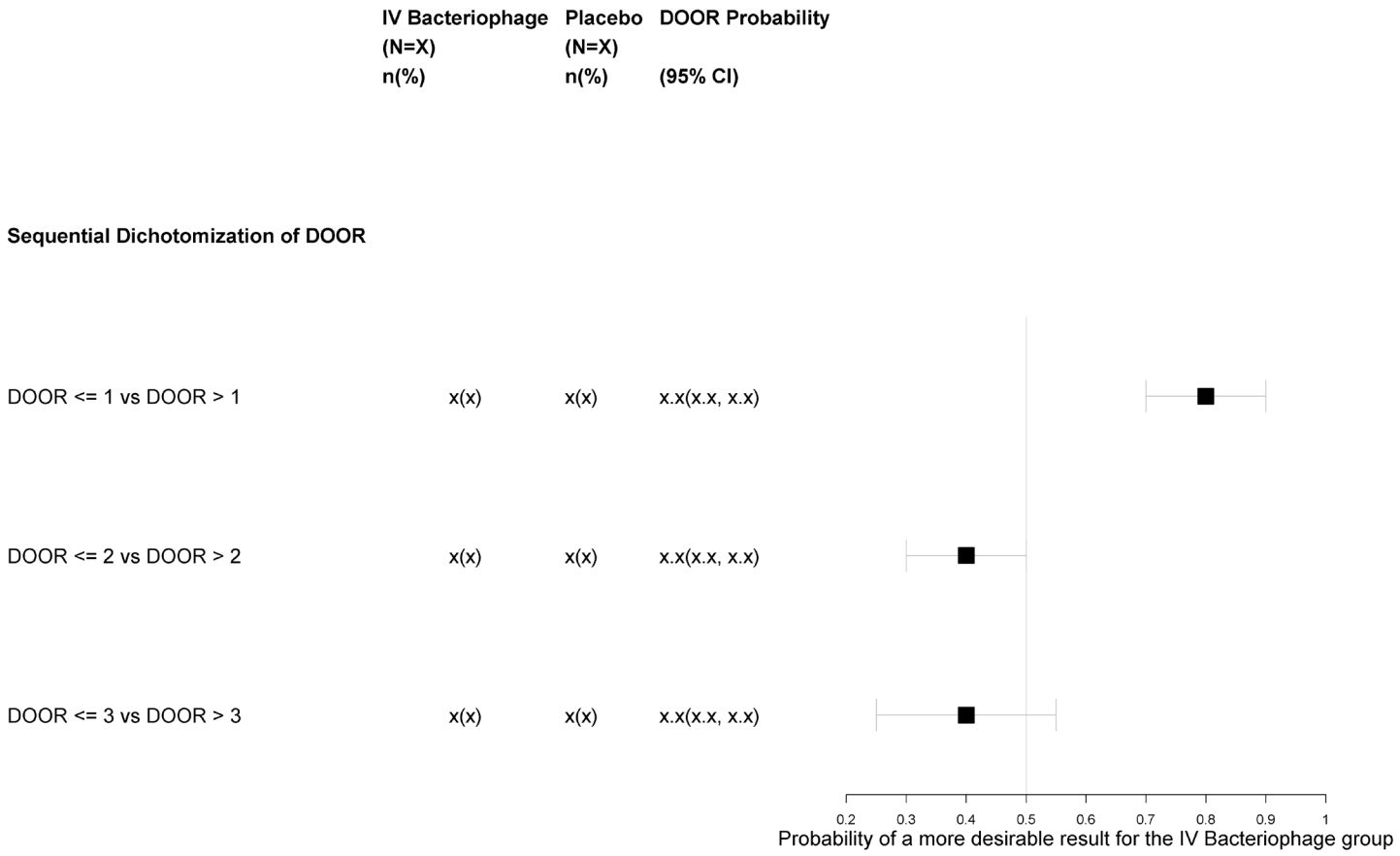


Figure with similar format:

Figure 16: Forest Plot of Sequential Dichotomization of DOOR Categories with 95% CI, Sensitivity Analysis

Figure 17: Difference in Means of Partial Credit Score by Time Point – ITT Population

[Implementation note: Change x-axis label to "Partial credit given DOOR Rank 3" and change y-axis label to "Partial credit given DOOR Rank 2".]

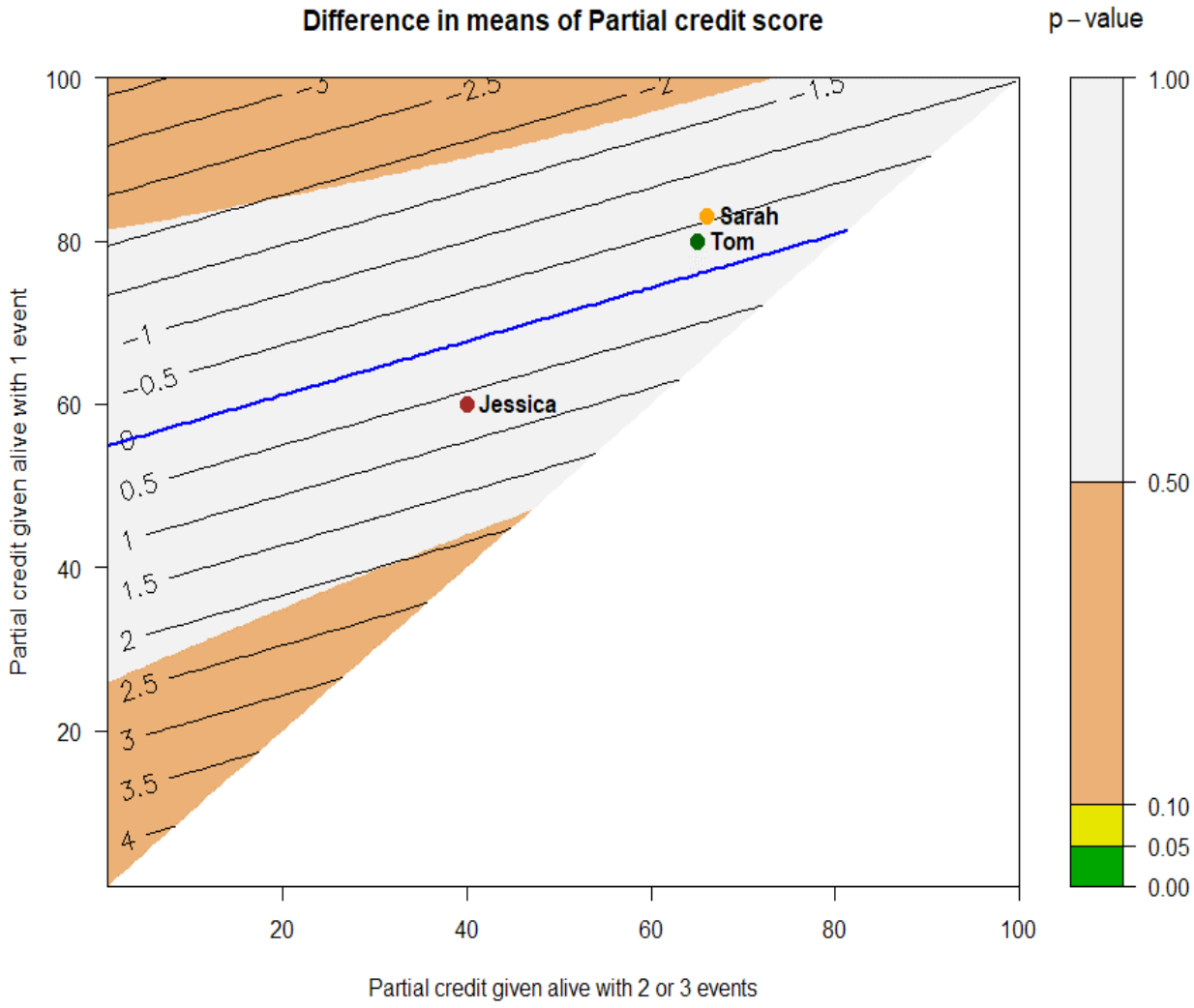
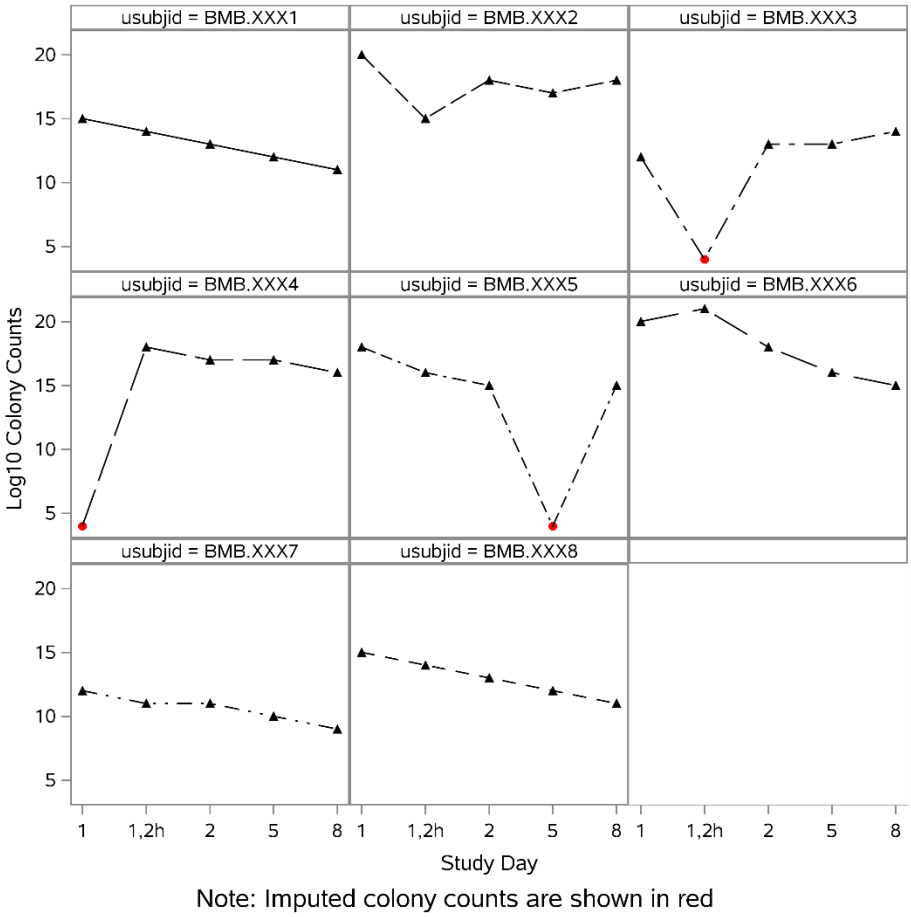


Figure with similar format:

Figure 18: Difference in Means of Partial Credit Score by Time Point – ITT Population, Sensitivity Analysis

Figure 19: Individual Log_{10} Colony Counts Through Day 8 – Stage 2a, 4 x 10^7 PFU Dose

[Implementation note: Substituted data points will be plotted in red circle. All other data points will use a black triangle.]



Figures with similar format:

Figure 20: Individual Log_{10} Colony Counts Through Day 8 – Stage 2a, 4 x 10^8 PFU Dose

Figure 21: Individual Log_{10} Colony Counts Through Day 8 – Stage 2a, 4 x 10^9 PFU Dose

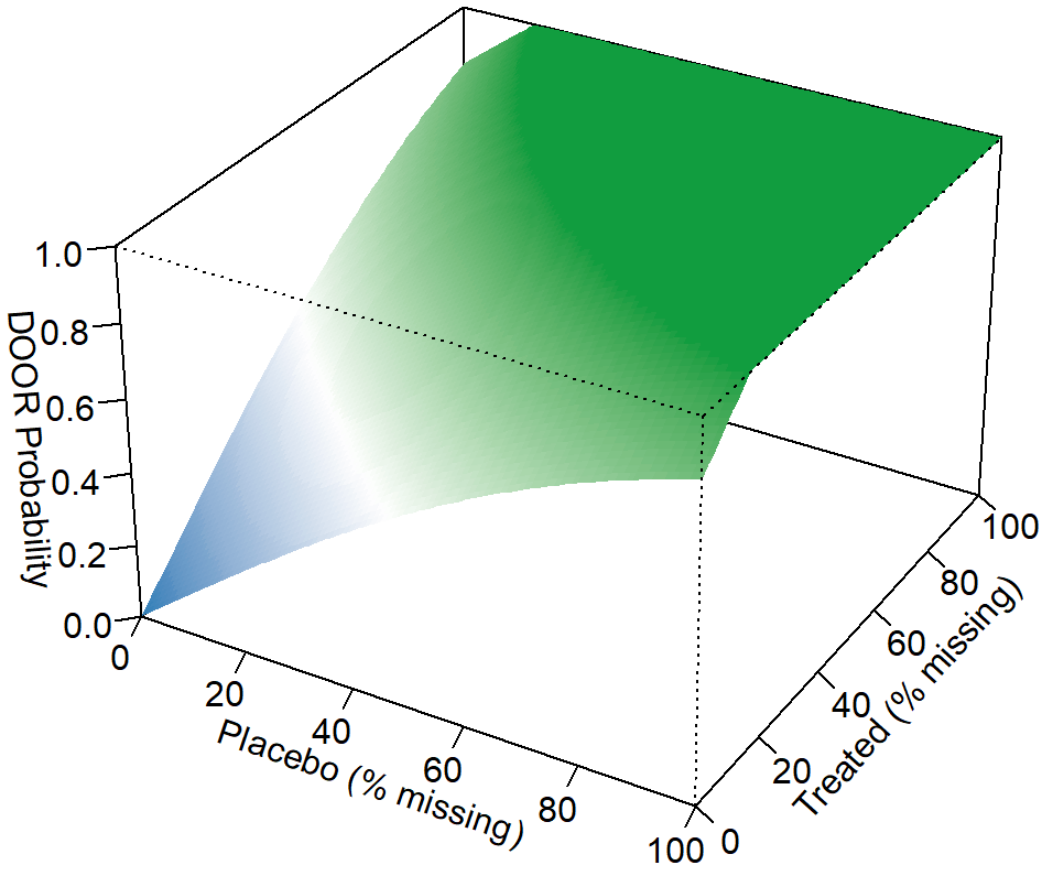
Figure 22: Individual Log_{10} Colony Counts Through Day 8 – Stage 2a, Placebo

Figure 23: Individual Log_{10} Colony Counts Through Day 8 – Stage 2b, 4 x 10^8 PFU Dose

Figure 24: Individual Log_{10} Colony Counts Through Day 8 – Stage 2b, Placebo

Figure 25: Tipping Point Visualization

[Implementation note: 'Treated' will be replaced with 'IV Bacteriophage']



APPENDIX 3. LISTINGS MOCK-UPS

LISTINGS

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Listing 2: Individual DOOR Response Data....57

16.2.6 Individual Microbiological Activity/Benefit to Risk Profile Response Data

Listing 1: **Listing of Colony Counts**

[Implementation Notes: Listing should be sorted by Treatment Group, Subject ID, and Planned Time Point. 'Other Organisms Recovered' field will concatenate the names of each organism recovered (if any) separated by a comma.

Substituted colony count values will be marked with an asterisk (*).]

Treatment Group	Subject ID	Planned Time Point	Other Organisms Recovered	Number of *P. aeruginosa* Morphotypes	Colony Count (CFU/mL)[a]	Log_{10} Colony Count (CFU/mL)
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 2			xx	xx
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 5			xx	xx

[a]Undetectable results are substituted as the LOD. Substituted colony count values will be marked with an asterisk (*).

Listing 2: Individual DOOR Response Data

[Implementation Notes: Listing should be sorted by Treatment Group, Subject ID, and Planned Time Point.]

Treatment Group	Subject ID	Planned Time Point	SAE Related to Study Product	Change in log_{10} Colony Counts from Baseline (CFU/mL)	DOOR Category	Sensitivity Analysis DOOR Category[a]
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 2	No	2	1	1
$4x10^7$ IV Bacteriophage	BMB.XXXX	Day 5	No	1	2	2

[a]Undetectable results are substituted as the LOD.