Statistical Analysis Plan Version 5.0

Official Title: A Phase 1 Trial to Evaluate the Safety, Immunogenicity, and Reactogenicity of a Self-Amplifying mRNA Prophylactic Vaccine Boost Against SARS-CoV-2 in Previously Vaccinated Healthy Adults 18 Years and Older

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Gritstone bio, Inc.

GO-009

A Phase 1 Trial to Evaluate the Safety, Immunogenicity, and Reactogenicity of a Self-Amplifying mRNA Prophylactic Vaccine Boost Against SARS-CoV-2 in Previously Vaccinated Healthy Adults 18 Years and Older

09JUN2023

Statistical Analysis Plan

Version 5.0

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Statistical Analysis Plan Revision History

Version	Date	Summary of Changes
Version 1.0	21MAR2022	Original version
Version 2.0	04MAY2022	- Amendment 1 (Version 2.0) of the SAP has been updated to add Cohorts 5 and 6, which will include younger subjects aged ≥18 to ≤59 years of age. To maintain the same total sample size, Cohorts 3 and 4 have each been reduced from 50 to 20 subjects. Additionally, blood sample collection has been added to Day 15 to better characterize the kinetics of antibody induction by the GRT-R910 vaccine. - Removed references to trial centers in the United States (US) and US-specific regulatory terms. - Removed language regarding thrombosis with thrombocytopenia syndrome (TTS) and vaccine induced immune thrombotic thrombocytopenia (VITT) as these are not applicable AESIs for this study. - Added urine or serum pregnancy est at screening for eligibility - Edited the window for Visit 7 (Day 113) to -3d/+21d.Added Section 9.1.1.8.- Adverse Events Leading to St dy Treatment Discontinuation. - Updated the language for Section 8.1 – Efficacy Analysis - Added birth control methods to list of demographics variables for DB modification - Added section 9.1 3 for study halting rules per DB modification
Version 3.0	11OCT2022	- Update to method of calculation for solicited AE's in section 9.1.2
Version 4.0	07MAR2023	- Redefined Pe -Protocol Set (PPS) and Immunogenicity Set (IMM) as separate analysis populations, and defined the immunogenicity analysis population flag as a pla eholder, as that analysis is outside of the scope of the current SAP - Replaced all references to CTCAE toxicity grading scale for clinical laboratory data with references to FDA toxicity grading guidance for healthy volunteers - Removed references to cohort 5 (removed from study in protocol v5 with 0 subjects treated) - Per revision in protocol v5, decreased the target sample size from 120 to 50. Removed references to cohort expansion. - Updated the Schedule of Assessments (Appendix 1) per protocol v5 - Other minor miscellaneous updates for alignment with protocol v5 - Added notes about handling of missing values for clinical laboratory values, vital signs, cardiac biomarkers, physical exams, and electrocardiograms - Redefined Major protocol deviation definiton to make it synonymous with the definition of Significant protocol deviation. - Section 9.2 updated to exclude shift tables for Coagulation labs to maintain consistency with the SoE.
Version 5.0	09JUN2023	- Added a second definition of COVID-19 incidence in section 8.1 Efficacy analysis - Added clarification about solicited adverse events collected from memory aid

List of Abbreviations

Abbreviation	Description
ACE-2	Angiotensin-Converting Enzyme 2
AE	Adverse Event
AES	All Screened Subjects Set
AESI	Adverse Event of Special Interest
ALP	ALP Alkaline Phosphatase
ALT	ALT Alanine Aminotransferase
aPTT	Activated Partial Thromboplastin Time
AST	AST Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
AZN	AstraZeneca's COVID-19 vaccine
BMI	Body Mass Index
BP	Blood Pressure
CI	Confidence Interval
cm	Centimeter
COVID-19	Coronavirus Disease 2019
CSR	Clinical Study Report
DCF	Data Collection Form
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ELISpot	Enzyme-Linked Immunospot
EUA	Emergency U e Authorization
FDA	Food and D ug Administration
HIV	Human Immunodeficiency Virus
IB	Investigator s Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
[redacted]	[redacted]
IFN	Interferon
IM	Intramuscular
IMM	Immunogenicity Set
INR	International Normalized Ratio
IR	Incidence Rate
ITT	Intent-To-Treat
kg	Kilogram
MAAE	Medically Attended Adverse Event
Max	Maximum
mcg	Microgram
MedDRA	Medical Dictionary for Regulatory Activities
MHRA	Medicines and Healthcare Products Regulatory Agency
Min	Minimum

Abbreviation	Description
MOP	Manual of Procedures
mRNA	Messenger Ribonucleic Acid
NA	Not applicable
NOCMC	New Onset Chronic Medical Conditions
PCR	Polymerase Chain Reaction
PD	Protocol Deviation
PI	Principal Investigator
PIMMC	Potentially Immune-Mediated Medical Conditions
PPS	Per-Protocol Set
PT	Preferred Term *(in Adverse Events section)*
PT	Prothrombin Time *(lab test)*
SAE	Serious Adverse Event
SAF	Safety Set
SAM	Self-Amplifying mRNA
SAP	Statistical Analysis Plan
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SAS	Statistical Analysis System
SDTM	Study Data Tabulation Model
SOC	System Organ Class
SUSAR	Suspected Unexpected Serious Adverse Reaction
TCE	T-cell epitopes
TEAE	Treatment-Emergent Adverse Events
TLF	Tables, Listings, Figures
WHO	World Health Organization

1. Introduction

As per ICH E9 [1], the main purpose of this document is to provide a more technical and detailed elaboration of the principal features of the analysis described in the protocol and to include detailed procedures for executing the statistical analysis.

This document outlines the statistical methods to be implemented in the analysis of the data collected within the scope of Gritstone bio, Inc., protocol GO-009 (a phase 1 trial to evaluate the safety, immunogenicity, and reactogenicity of a self-amplifying mRNA prophylactic vaccine boost against SARS-CoV-2 in previously vaccinated healthy adults 18 years and older), Version 5.0, dated 09 February 2023.

The purpose of this open label, multiple cohorts, dose-escalation, Phase 1 vaccine trial is to evaluate the safety, immunogenicity, and reactogenicity of a self-amplifying mRNA boost prophylactic vaccine against SARS-CoV-2 in previously vaccinated healthy adults 18 years and older (subjects). The primary objective of this study is to assess the safety and tolerability of two different doses (10 or 30 mcg) of GRT-R910 when administered as boost in healthy adult volunteers (≥ 18 years) who were previously vaccinated with a first-generation Coronavirus Disease 2019 (COVID-19) vaccine (Cohorts 1 and 2; AstraZeneca), an adenoviral COVID-19 vaccine (AstraZeneca, Janssen), or an mRNA-based COVID-19 vaccine (Pfizer/BioNTech, Moderna).

The purpose of this statistical analysis plan (SAP) is to define the planned statistical analysis of the study data consistent with the safety study objectives. Therefore, analysis for immunogenicity will be described in a separate SAP.

References throughout this SAP to specific visits by study day (e.g., Day 1) refer to study day as defined in schedule of events in Appendix 1.

2. Objectives and Endpoints

Objectives	Endpoints (Outcome Measures)
Primary	
• To assess the safety and tolerability of 2 different doses (10 or 30 mcg) of GRTR910 when administered to healthy adults ≥60 years of age who were previously vaccinated with a first-generation COVID-19 vaccine (Cohorts 1 and 2; AstraZeneca) • To assess the safety and tolerability of a 10 mcg dose of GRT-R910 when administered to healthy adults (≥18 years of age) who were previously vaccinated with either an adenoviral COVID-19 vaccine (AstraZeneca, Janssen) or an mRNA-based COVID-19 vaccine (Pfizer/BioNTech, Moderna)	• Occurrence of solicited local reactogenicity signs and symptoms for 7 days after GRT-R910 vaccination • Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days after GRT-R910 vaccination • Occurrence of unsolicited AEs for 28 days after last study-administered GRT-R910 vaccination • Change from baseline for clinical safety laboratory parameters 7 days after last study-administered GRT-R910mvaccination • Occurrence of SAEs and adverse events of special interest (AESIs), including potentially immune-mediated medical conditions (PIMMCs), medically attended adverse events (MAAEs), and new onset chronic medical onditions (NOCMCs), throughout the entire study after GRTR910 vaccination
Secondary	
• To assess the cellular and humoral immunogenicity of GRT-R910 when administered to volunteers (≥60 years of age for C horts 1, 2, 3, and 4 and ≥18 to ≤59 years of age for Cohort 6) who were previously vaccinated with either an adenoviral COVID-19 vaccine (AstraZeneca, Janssen) or an mRNA-based COVID-19 vaccine (Pfizer/BioNTech, Moderna)	• Response rate, and magnitude of SARSCoV-2-specific antibody binding and neutralization in serum samples. • Response rate, magnitude, and breadth of SARS-CoV-2 specific T-cells as assessed by interferon (IFN)-enzyme-linked immunospot (ELISpot) for 10 subjects per cohort
[redacted]	
[redacted]	

[redacted]

3. Investigational Plan

3.1. Overall Study Design and Plan

Overall Design

This is a multi-center, open-label, dose-escalation design study to examine dose, safety, tolerability, and immunogenicity of GRT-R910, an investigational SAM SARS-CoV-2 vaccine when administered to healthy adults 18 years and older who were previously vaccinated with a first generation COVID-19 vaccine (Cohorts 1 and 2; AstraZeneca), an adenoviral COVID-19 vaccine (Cohort 3; AstraZeneca, Janssen), or an mRNA-based COVID-19 vaccine (Cohorts 4 and 6; Pfizer/BioNTech, Moderna). See the study flow chart is shown in Figure 1.

In Cohorts 1 and 2, healthy adults ≥60 years of age (N=10, including 2 sentinels per cohort) will receive 2 doses of GRT-R910 (homologous prime boost) at 1 of 2 dose levels (10 mcg or 30 mcg) at least 2 months after receiving AstraZeneca's COVID-19 prime and boost vaccine. The GRT-R910 booster dose will be administered 113 days (16 weeks) after the prime. In Cohorts 3 and 4, healthy adults ≥60 years of age (N=10) will receive 2 doses of GRT-R910 (homologous prime-boost) 10 mcg (dose selected from Cohorts 1 and 2) at least 2 months after receiving an adenoviral COVID-19 vaccine (Cohort 3; AstraZeneca, Janssen), or an mRNA-based COVID-19 vaccine (Cohort 4; Pfizer/BioNTech, Moderna). In Cohort 6, healthy adults ≥18 to ≤59 years of age will receive 2 doses of GRT-R910 (homologous prime-boost) 10 mcg (dose selected from Cohorts 1 and 2) at least 2 months after receiving an mRNA-based COVID-19 vaccine (Pfizer/BioNTech, Moderna). The GRT-R910 booster dose will be administered 28 days after the prime.

Sentinel dosing in Cohorts 1 and 2 will consist of 2 volunteers in each cohort dosed 72 hours ahead of the remainder of each cohort, with the remainder of the volunteers dosed at the same dose level only if no halting rules are met (Section 11.7 of the protocol [2]). Enrollment in Cohort 2 will only proceed if safety data from all volunteers in Cohort 1 meet the dose-escalation rules. There will be no sentinel dosing in Cohorts 3 ,4, and 6. The dose for Cohorts 3, 4, and 6 was selected from Cohorts 1 and 2 after evaluation of reactogenicity, safety, and initial immunogenicity. Dose selection will be determined by the Gritstone clinical team in consultation with the PI(s).

The reactogenicity and immunogenicity data assessed after the first dose of GRT-R910 will inform selection of the GRT-R910 dose to be tested in future studies. The 10 mcg dose of GRTR910 was selected for use in Cohorts 3, 4, and 6 by evaluating the balance of immunogenicity and reactogenicity of a single dose of GRT-R910 in Cohorts 1 and 2.

This study will enroll 50 volunteers as follows:

- Cohort 1 (N=10, including 2 sentinels): 10 mcg GRT-R910 (after AstraZeneca) 2 doses, homologous prime-boost, booster dose will be 113 days (16 weeks) after the prime for healthy adults ≥60 years of age.
- Cohort 2 (N=10, including 2 sentinels): 30 mcg GRT-R910 (after AstraZeneca) 2 doses, homologous prime-boost, booster dose will be 113 days (16 weeks) after the prime for healthy adults ≥60 years of age.
- Cohort 3 (N=10): 10 mcg GRT-R910 (dose selected from Cohorts 1 and 2) after adenovirus based vector vaccine, homologous prime-boost, booster dose will be 28 days after the prime for healthy adults ≥60 years of age.
- Cohort 4 (N=10): 10 mcg GRT-R910 (dose selected from Cohorts 1 and 2) after messenger ribonucleic acid (mRNA) vaccine, homologous prime-boost, booster dose will be 28 days after the prime for healthy adults ≥60 years of age.
- Cohort 6 (N=10): 10 mcg GRT-R910 after messenger ribonucleic acid (mRNA) vaccine (dose selected from Cohorts 1 and 2), homologous prime-boost, booster dose will be 28 days after the prime for healthy adults ≥18 to ≤59 years of age.

Follow-up duration after the Prime dose

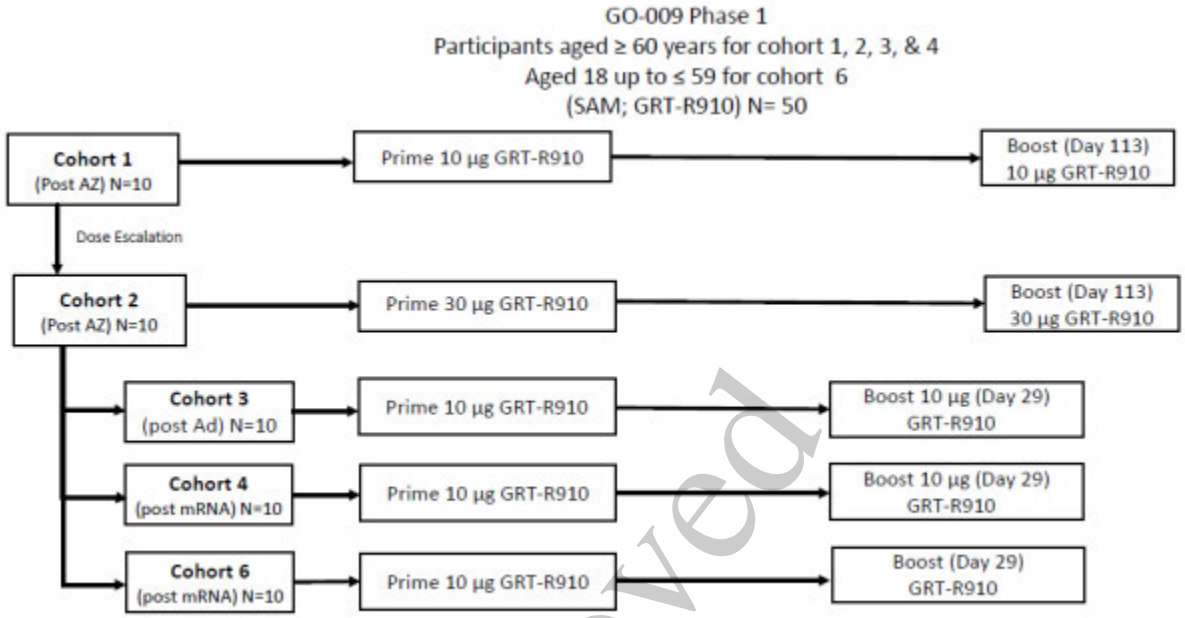
- For Cohorts 1 and 2 (NOT receiving booster dose): 12 months
- For Cohorts 1 and 2 (receiving booster dose): 16 months
- For Cohorts 3, and 4: up to 13 months
- For Cohort 6: 7 months

End of Study Definition

All subjects will be followed up to 12 months after the boost vaccination or prime dose for subjects not consenting to booster vaccination. Vaccinated subjects will be carefully monitored for exposure and infection to SARS-CoV-2 throughout the study.

The schedule of events is provided in Table 6, Table 7, and Table 8 (Appendix 1).

Figure 1 Study Flow Chart



3.2. Treatments

The following dosing and administration rules will be applied to this study (Table 1):

Table 1 Dosing and Administration

Cohort	N	GRT-R910 Prime Day 1	GRT-R910 Boost 113 days (16 weeks [-3d/+21d]) after prime
1[a]	10[b]	10 mcg	10 mcg
2[a]	10[b]	30 mcg	30 mcg
	N	**GRT-R910 Prime Day 1**	**GRT-R910 Boost 28 days after prime**
3[c]	10	10 mcg[d]	10 mcg
4[c]	10	10 mcg[d]	10 mcg
6[e]	10[e]	10 mcg[d]	10 mcg
TOTAL	**50**		

a Healthy adults aged ≥60 years at least 2 months after receiving AstraZeneca's COVID-19 prime and boost vaccine.

b Cohort will include 2 sentinel subjects.

c Healthy adults aged ≥60 years at least 2 months after receiving an adenoviral COVID-19 vaccine (Cohort 3) or an mRNA based COVID-19 vaccine (Cohort 4).

d Dose selected from Cohorts 1 and 2.

e Healthy adults ≥18 to ≤59 years of age at least 2 months after receiving an mRNA based COVID-19 vaccine (Cohort 6).

4. General Statistical Considerations

All data collected will be presented in data listings sorted by cohort and subject, and when appropriate by study days number within subject. Data from subjects excluded from an analysis

set will be presented in the data listings but not included in the calculation of summary statistics for that analysis set.

Summary statistics for continuous variables will include the number of patients/observations (n), mean, standard deviation, median, minimum, and maximum. Categorical data will be summarized by cohort using frequency and percentages. Unless otherwise stated, the denominator of percentages will be the number of participants in the population of interest and cohort. The number of missing values will be presented as a separate category but will only be displayed if one or more subjects are missing data. Counts of zero will be presented without percentages.

Any additional exploratory analysis not defined in the SAP will be identified in the final CSR as exploratory post hoc analysis, including analyses for additional study populations or subgroups of interest.

All data processing, summarization, and analyses will be performed using SAS Environment/ Version 9.4 or later of the SAS® statistical software package [3]

Unless otherwise stated, the principles below will be applied:

4.1. General considerations

4.1.1. Visit windows

These rules will be followed during the study:

- If there is no overlapping in visit windows according to the protocol, no additional visit windows will be applied to this study.
- If there is an overlapping of visit windows (e.g., V07 and V08 for Cohorts 1 and 2 receiving the Booster dose, V06 and V07 for Cohorts 3, 4, and 6), the visit when a subject took the vaccine will be the targeted V07 or V06, respectively. All assessments made in the next 1 or 2 days will be allocated as V08 and V07, respectively.

4.1.2. Repeat/unscheduled assessments

Additional exams may be scheduled as necessary to ensure the safety and well-being of subjects who experience AEs during the study. Any additional examinations during the study will be fully documented in the source documents and Unscheduled Visit eCRF.

Multiple visits within the same window will be dealt with for all populations as follows:

- In case the unscheduled visit was performed on or before the vaccination, so they can be considered to calculate the baseline value, the following rules will be applied:
  - If dates of visits (scheduled and/or unscheduled) are known and different, then the latest visit will be taken.
  - If date and time of visits are known and different, then the latest visit will be taken.
  - If dates of visits are the same, and time is not known, then latest visit based on SDTM sequence number will be taken.

- If data corresponding to an unscheduled visit met the baseline record selection criteria or when selecting the worst case in shift tables.

- If the unscheduled visit was performed after vaccination, the following rules will be applied:
  - If both scheduled and unscheduled visits fall within the same visit window, the scheduled visit will be used for analysis.
  - If one or multiple unscheduled visits occur within a single visit window without scheduled visit, no data will be used in the by-visit summaries of data analysis. If there are multiple unscheduled visits occur within a single visit window with ties, the later unscheduled visit will be used in the data listings.

4.1.3. Missing data

All data will be analyzed as collected and missing values will n t be imputed or replaced.

For the classification of treatment-emergent adverse even s (TEAEs) and concomitant medication, the following imputation rules will be applied in a hierarchical order:

- If no start/end date information is available (i.e., no day, month, or year is available), the event/medication will automatically be classified as a TEAE/concomitant medication/ procedure. AEs with a missing start time occurring on the day of vaccination will be set to a TEAE unless the end time of the event is before the vaccination time.
- For AEs/concomitant medications if only the event start year/end year is present and the start/end year is the same or after the year of the vaccination, then the event/medication will be classified as a TEAE/concomitant medication.
- If only the event/medication start/end year and month are present and the start/end year and month is the same or after the month and year of the date of the vaccination, then the event/medication will be cl ssified as a TEAE/concomitant medication.

4.1.4. Multi-center studies

This is a multi-center trial in the United Kingdom. Data obtained at all sites will be combined into one data set prior to statistical analysis.

4.1.5. Multiple comparisons/Multiplicity

So far as no specific statistical hypothesis will be tested and only safety data will be evaluated, multiple adjustments are not applicable for this study.

4.2. Key definitions and principles

The following principles and definitions will be applied to all tables, listings, and figures (TLFs), unless otherwise specified, are described in Table 2.

Table 2 Principles and definitions for all tables, listings, and figures

Principle/definition	Value
Baseline	Is defined as the last available valid, non-missing observation for each subject on or before the vaccination of the prime dose at *V01/Day 1*. Repeat and unscheduled assessments will be included in the derivation of the baseline values.
Change from Baseline	Is defined as difference between the results collected/derived at a post-baseline visit and baseline value. The change from baseline value at each post-baseline visit will be calculated for continuous parameters using the following formula: *Change from baseline = (Result at post-baseline visit) – (Baseline value)* The change from baseline value will only be calculated if the specific post-baseline visit/time point result and the baseline value for the parameter are both available and will be treated as missing otherwise. In the data listings, the change values will be set to 'N/A' (not applicable) for pre-baseline assessments.
Study Day	Is defined as the relative day of the event starting with the date of vaccination of the prime dose (the reference day) as Day 1 (there will be no Day 0). The study day of events occurring before the vaccination of the prime dose will be calculated in the following way: *Study day (before vaccination) = (Date of event) – (Date of Vaccination of Prime Dose)* For events occurring on or after the vaccination will be calculated as: *Study day (after vaccination) = (Date of event) – (Date of Vaccination of Prime Dose) + 1* Study days will only be calculated for events with complete dates and will be undefined for event that are 'Ongoing' at the end of the study.
Display Convention of Results	Results will be center-aligned in all summary tables and left-aligned in all listings. Subject identifiers, visits, parameter labels, and comments may be left-aligned if required.
Descriptive Summary Statistics for Continuous Variables	Descriptive statistics will include the number of non-missing values (n), arithmetic mean, standard deviation (SD), median, minimum (min), and maximum (max) values. The minimum and maximum values will be displayed to the same decimal precision as the source data; the arithmetic mean, median, values will be displayed to one more decimal than the source data, and the SD values will be displayed to two more decimals than the source data for the specific variable. The maximum number of decimal places in the statistical report is four. If some descriptive statistical value has more than four decimal places after the application of the above-mentioned rules, this value will be rounded to four decimal places. The appropriate precision for derived variables will be determined based on the maximum precision of the data on which the derivations are based, and statistics will be presented following the above-mentioned rules.
Descriptive Summary Statistics for Categorical Variables	Descriptive statistics will include frequencies and percentages per category as well as clinical evaluations (normal, abnormal, and not clinically significant, abnormal, and clinically significant). The denominator in all percentage calculations will be the number of subjects in the relevant analysis population in the corresponding treatment group with non-missing data unless specifically stated otherwise. Percentages will be rounded to one decimal place
Significance Test	The default significance level will be 0.05 (5%); all tests are two-sided (where applicable) unless otherwise specified in the description of the analysis.
Confidence Intervals (CIs)	The default CIs will be 95% and will be determined using the Clopper-Pearson method [6].

Principle/definition	Value
p-values	All p-values will be presented to 3 decimal places and values less than 0.001 or greater than 0.999 will be presented as <0.001 and >0.999, respectively.

4.3. Sample Size

The targeted sample size for each of the study cohorts was determined based on previous Phase 1 studies. Recruitment for GRT-R910 boost vaccination schedules will target enrolling 50 volunteers as follows:

- Cohort 1 (N=10, including 2 sentinels): 10 mcg GRT-R910 (after AstraZeneca) 2 doses, homologous prime-boost, booster dose will be 113 days (16 weeks) after the prime for adults ≥60 years of age.
- Cohort 2 (N=10, including 2 sentinels): 30 mcg GRT-R910 (after AstraZeneca) 2 doses, homologous prime-boost, booster dose will be 113 days (16 weeks) after the prime for adults ≥60 years of age.
- Cohort 3 (N=10): 10 mcg GRT-R910 (dose selected from Cohorts 1 and 2) after adenovirus-based vector vaccine, homologous prime-boost, booster dose will be 28 days after the prime for adults ≥60 years of age
- Cohort 4 (N=10): 10 mcg GRT-R910 (dose selected from Cohorts 1 and 2) after mRNA vaccine, homologous prime-boost, booster dose will be 28 days after the prime for adults ≥60 years of age.
- Cohort 6 (N=10): 10 mcg GRT R910 (dose selected from Cohorts 1 and 2) after mRNA vaccine, homologous prime-boost, booster dose will be 28 days after the prime for adults ≥18 to ≤59 years of age.

Sample size and power analysis for safety

The goal of the safety evaluati n for this study is to identify safety concerns associated with product administration. The ability of the study to detect serious adverse events (SAEs) (see Section 11.1.2 of the protocol [2]) can be expressed by the true event rate above which at least 1 SAE would likely be observed.

For each group of 10 subjects, there is an 89% chance of observing at least 1 event if the true rate is 20% or higher.

Binomial probabilities of observing at least 1 event among groups of size 10 overall are presented in Table 3 for a range of possible true adverse event rates [4]. These calculations provide a more complete picture of the sensitivity of the study design to identify potential safety problems with the vaccine.

Table 3 Probability (%) to Detect at Least 1 Adverse Event Under Different Incidence Rate

Incidence Rate (%)	Sample size = 10	Sample size = 20	Sample size = 30
0.01	0.10	0.20	0.30
0.1	1.00	1.98	2.96
1.0	9.56	18.21	26.03

Incidence Rate (%)	Sample size = 10	Sample size = 20	Sample size = 30
2.0	18.29	33.24	45.45
5.0	40.13	64.15	78.54
10.0	65.13	87.84	95.76
20.0	89.26	98.85	99.88

4.4. Randomization, Stratification, and Blinding

Since this is an open-label Phase 1 study, no randomization, stratification in randomization, or blinding will be performed. Thus, subjects and site staff will be unblinded as to subjects' cohort assignments.

4.5. Analysis Set

4.5.1. All Screened Subjects (AES)

The All Screened Subjects Analysis Set (AES) will contain all subjects who sign informed consent for this study. The subject screening and enrollment tables and listings will be reported using AES.

4.5.2. Intent-to-Treat (ITT)

The Intent-to-Treat Analysis Set (ITT) set will contain all subjects in AES who was not marked as screen failures. Subjects in the ITT analysis set will be analyzed according to the treatment assignment. The disposition tables and listings will be reported using ITT.

4.5.3. Safety Analysis Set (SAF)

The Safety Analysis Set (SAF) will contain all subjects in AES who received at least 1 dose of GRT-R910.

Summaries and analysis of safety data will be presented for the Safety Analysis Set. Subjects will be analyzed according to their actual treatment.

4.5.4. Immunogenicity Set (IMM)

The Immunogenicity Analysis Set (IMM) will contain all subjects in AES who received at least 1 dose of GRT-R910. For purposes of this SAP, it will be synonymous with SAF. However, further definition of the IMM set may be provided at a later time, as the immunogenicity analysis will be described in a separate standalone SAP, and performed by the sponsor.

4.5.5. Per Protocol Set (PPS)

The Per-Protocol Set (PPS) contains all subjects in ITT who received at least 1 dose of Investigational product (IP), with no major protocol violations. The major protocol violations that impact the Per-Protocol Set are detailed in the study deviation rules document. Prior to database lock, the sponsor will review the protocol deviations and categorize into minor or major protocol deviations and finalize the protocol deviations

Subjects will be analyzed according to their treatment assignment.

5. Subject Disposition

5.1. Subject Disposition

Subject screening and enrollment status will be summarized via AES; below information will be provided:

- Screened
- Enrolled - Enrolled represented the number of subjects who passed screening.
- Screen Failed
- Treated
- In Cohort 1 and 2 Consented to Booster Period

Subject disposition will be summarized by treatment cohort and total for the ITT using descriptive statistics (frequency and percentages).

The following characteristics will be summarized as subject disposition for the ITT:

- Number of subjects:
  - Completed the study
  - Discontinued the study
  - Ongoing
- Primary reason for discontinuation from th study and study drug
- Number of subjects in:
  - Safety Analysis Set
  - Immunogenicity Analysis Set
  - Per Protocol Immunogenicity Set

Also, the characteristics will be reported via data listing for the ITT.

5.2. Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol, any process that is noted in the protocol and refers to details in the protocol-specific manual of procedures (MOP) or GCP requirements, or any critical study procedures with specific instructions in ancillary documents referenced in the protocol such as a protocol-specific MOP.

Subject data will be examined for evidence of protocol deviations (PDs) to assess the protocol compliance. They are captured in the electronic data capture (EDC) system.

Before any reporting, each PD will be marked as major or minor. A major protocol deviation is considered synonymous to a significant deviation. A major protocol deviation is defined as a protocol or ICH/GCP deviation that affects the primary efficacy assessment, the safety or mental integrity of a subject, or the scientific value of the trial. A major protocol deviation can include nonadherence to inclusion or exclusion criteria or nonadherence to regulatory authority including International Council for Harmonization E6 (R2) [5] guidelines.

Major protocol deviations will be summarized by cohort and total for the ITT set using descriptive statistics (frequency and percentages).

All protocol deviations will be presented in a data listing, including the categorization of the deviation as important or not. Details of admission criteria deviations will be presented in a separate data listing. The significance of all protocol deviations will be determined by the sponsor.

6. Demographics and Baseline Characteristics

6.1. Demographics

Demographics will be summarized by cohort and total for the SAF analysis set using descriptive statistics.

The following data will be summarized:

- Age
- Sex
- If a female subject is Post-menopausal (percentages will be based on the number of female subjects)
- If a female is of child-bearing potential (percentages will be based on number of female subjects from cohort 6)
- If a female subject is of child-bearing potential, agreement to use of contraception on study per section 7.1 of the protocol
- If a female subject is of child-bearing potential, methods of contraception used
- Ethnicity
- Race
- Height (cm)
- Weight (kg)
- BMI (kg/m^2)

BMI will be calculated using the following formula: $BMI[\frac{kg}{m^2}] = \frac{WEIGHT[kg]}{(HEIGHT[cm]/100)^2}$.

Also, all parameters will be reported in a data listing for the SAF.

6.2. Baseline Disease Characteristics

The results of Nasal Swab SARS-CoV-2 PCR test will be summarized and reported via a data listing for the SAF.

6.3. Medical History

6.3.1. General Medical History

Medical history will be assessed at the Screening visit and then before GRT-R910 vaccination to ensure continued eligibility. Also, the medical history will be reviewed during the study to be sure that no changes took place since the previous clinic visit, phone call or other form of contact. The

interim medical history should include an assessment for new medical conditions and symptoms suggestive of an autoimmune disorder.

Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) version to be delineated in the CSR.

Medical history will be summarized by SOC and PT within treatment group and total for the SAF. Additionally, medical history will be presented in a data listing.

No data will be imputed.

6.4. Inclusion and Exclusion Criteria

The inclusion/exclusion criteria will be reported by a data listing for the AES.

7. Treatments, Medications, and Recent Vaccinations

7.1. Prior and Concomitant Medications, and Recent Vaccinations

Administration of any medications, therapies or vaccines will be recorded on the appropriate DCF. Concomitant medications will include all current medications and medications taken in the 30 days prior to signing the ICF for the duration of the study. Medications reported in the electronic case report form (eCRF) are limited to those taken within 30 days prior to the first study vaccination and for 12 months after GRT-R910 vaccination. Prescription and over the counter drugs will be included as well as herbals, vitamins, and supplements. In addition, receipt of any non-study vaccines will be solicited for the entire duration of the study and reported in the eCRF.

Medications that might interfere with th evaluation of GRT-R910 should not be used during the trial reporting period (until approximately 12 months after GRT-R910 vaccination) unless clinically indicated as part of the subject's health care.

Recent vaccinations and concomitant medications and therapies will be summarized for the SAF by treatment group, anatomical therapeutic chemical (ATC) levels 1 and 2 and Preferred drug names as coded using the World Health Organization Drug Dictionary (version to be delineated in the CSR).

Additionally, any COVID-19 Emergency Use Authorization (EUA) will be recorded in CRF. If an EUA was reported, the usage of this medication should be considered as a major protocol deviation. Also, the case will be reviewed further to decide if subject will still stay on the study.

The rules for dates imputations described in Table 4 will be applied to concomitant medications during this study. No other data will be imputed.

Table 4 Algorithm for missing dates imputations

Missing Date Type	Missing Date Description	Action
Start date	YYYY-MMM-UK	Assume YYYY-MMM-01, but if month and year are the same as the first study vaccination month and year, then assume the date of first vaccination

Missing Date Type	Missing Date Description	Action
	YYYY-UNK-UK	Assume YYYY-JAN-01, but if year is the same as the first study vaccination year, then assume the date of first study vaccination
	UNKN-UNK-UK	Assume the date of first study vaccination
Stop Date	YYYY-MMM-UK	Assume the last day of the month
	YYYY-UNK-UK	Assume YYYY-DEC-31
	UNKN-UNK-UK	Assign as 'Ongoing'

All concomitant medications and recent vaccinations will be reported via data listings. No partial dated will be imputed if the concomitant medications are considered as COVID-19 EUA; data queries will be sent to site to collect complete dates.

7.2. Study Vaccine Administration

Depending on the Cohort, study vaccination will be comprised of one or two intramuscular (IM) injections in the deltoid muscle of the subject's preferred arm. For Cohorts 1 and 2, initially subjects began the study only planning to receive one dose. In order to receive a booster dose, each subject needed to sign another ICF.

The number of doses received will be summarized for the SAF using descriptive statistics for qualitative variables. In addition, the vaccine administration data will be presented in a data listing.

8. Efficacy and Immunogenicity Analysis

8.1. Efficacy analysis

COVID-19 incidence in subjects will be assessed using two separate metrics. The number and percentage of subjects who had (1) a positive nasal swab SARS-CoV-2 PCR test during the study and (2) an Adverse Event with a MedDRA preferred term of "COVID-19", "Asymptomatic COVID-19", or "COVID-19 pneumonia" will be summarized for the SAF.

For both measures, the incidence rate (IR) is defined as the number of subjects with an event divided by the number of subjects at risk and person-days adjusted by person-years (total time at risk). The IR's of subjects with (1) positive PCR and (2) MedDRA preferred terms indicating COVID-19 will be reported in the fashion of 100 person-years (see the formula below).

$$IR = \frac{number\ of\ subjects\ with\ positive\ PCR}{sum(Person - days\ at\ risk)} * 365.25 * 100$$

Person-Days at risk are defined as the total time from injection date of prime dose to the date of the positive PCR test for (1) or AE start date for (2), last date of study participation, data cutoff date, whichever is the earliest. The respective 95% CIs of positive nasal swab SARS-CoV-2 PCR tests and COVID-19-related adverse events will be calculated using the Clopper-Pearson [6] method.

8.2. Immunogenicity Analysis

Not applicable for this statistical analysis plan and will be described in a separate SAP.

9. Safety Analysis

All safety summaries and analyses will be conducted for the Safety Analysis Set.

Safety data will be presented by actual treatment received at Prime dose (prior to Booster) and by actual Booster dose received (on or after Booster).

Safety will be assessed by the frequency and severity of:

- SAEs occurring after signing of the informed consent form (ICF) throughout the entire study.
- Solicited AEs (reactogenicity events occurring from the time GRT-R910 vaccination through 7 days after GRT-R910 vaccination).
- Reactogenicity local reactions (including erythema, induration/edema, pain, and tenderness).
- Reactogenicity systemic reactions including fever, chills, fatigue, malaise, myalgia, arthralgia, headache, and nausea.
- Clinical safety laboratory AEs occurring from the time of GRT-R910 vaccination through approximately 7 days after GRT-R910 vaccination. Parameters to be evaluated include WBC, Hb, PLT, ALT, AST, ALP, total bilirubin, CK, and creatinine.
- Unsolicited AEs (non-serious AEs occurring from the time of GRT-R910 vaccination through approximately 28 days after GRT-R910 vaccination).
- AESIs (including serologically r virologically confirmed SARS-CoV-2 infection and severity of COVID-19 and th ombosis with PIMMCs, MAAEs, and NOCMCs occurring from the time of the first study vaccination throughout the entire study) [2].

Assessments of cardiac bioma kers (see 9.4), body system evaluations through physical exams (see 9.5), and electrocardiograms (ECG; section 9.6) will also be used to assess safety. Interpretations that are missing or otherwise not done will be reported as counts, but will not be included in the denominator.

9.1. Adverse Events

Adverse Event (AE) means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related in a patient or clinical investigation subject administered a pharmaceutical product regardless of its causal relationship to the study treatment.

An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporarily associated with the use of a medicinal (investigational) product. The occurrence of an AE may come to the attention of study personnel during study visits and interviews of a study recipient presenting for medical care, or upon review by a study monitor. AEs, including solicited local and systemic (subjective and quantitative) reactions, not meeting the protocol-defined criteria for SAEs will be recorded on the appropriate DCF and entered into the

eCRF. Information to be collected for unsolicited non-serious AEs includes event description, date of onset, licensed study physician's assessment of severity and relationship to GRT-R910 or alternate etiology (if not related to study product) (assessed only by those with the training and authority to make a diagnosis (date of resolution, seriousness, and outcome. AEs occurring during the trial collection and reporting period will be documented appropriately regardless of relationship to GRT-R910. AEs will be followed through resolution.

Any medical condition that is present at the time that the subject is screened will be considered as baseline and not reported as an AE. However, if the severity of any pre-existing medical condition increases, it should be recorded as an AE.

A treatment-emergent AE (TEAE) is defined as any new AE that begins after the first vaccination or any pre-existing condition that worsens in severity. A treatment related adverse event (TRAE) is defined as any AE that is deemed to be related to the vaccination.

Adverse events consist of solicited AEs (local and systemic), unsolicited treatment-emergent AEs, treatment-related AEs, severe AEs, SAEs, MAAEs, AESIs, AEs leading to withdrawal from study participation.

All AEs will be coded using the MedDRA (version to be delineated in the CSR), including System Organ Class (SOC) and Preferred Term (PT) names. Summary by SOC and PT will be shown in some tables. The data will also include AEs based on laboratory assessment (if applicable). All AEs will be followed through resolution.

Only TEAEs will be included in summary tabl s and will be summarized by cohort and vaccination (Vaccination Dose 1, Vaccination Dose 2, entire study period). Percentages will be based upon the number of participants in the Safety Analysis Set within each cohort. A subject may have more than 1 AE for an SOC or PT. A subject with 2 or more AEs within the same level of summarization will be counted only once in that lev l

The rules described in Table 4 will be applied for AEs partial dates during this study to understand if it is TEAE. No other data will be imputed.

All AEs will be reported by data listings for the SAF.

9.1.1. Unsolicited Adverse Events

Unsolicited non-serious AEs will be captured for 28 days following each GRT-R910 vaccination. Unsolicited adverse events may be recorded beyond 28 days, but only AEs occurring within 28 days of treatment vaccination will be summarized. In addition, SAEs and AESIs, including PIMMCs, MAAEs, and NOCMCs, will be captured throughout the entire study following GRT-R910 vaccination.Incidence of Unsolicited Adverse Events

An overall summary of unsolicited TEAEs through 28 days after GRT-R910 vaccination (1st dose and/or booster dose) including the number and percentage of subjects who experienced the following will be presented:

- Any unsolicited TEAEs
- Any unsolicited Treatment-Related TEAEs

- Any serious TEAEs
- Any serious Treatment-Related TEAEs
- Any unsolicited severe TEAEs
- Any Treatment-Related severe TEAEs
- Any unsolicited AESIs

An overall summary of the following AEs will be presented throughout the entire study:

- Any serious AEs
- Any unsolicited medically attended TEAEs (MAAEs)
- Any unsolicited AESIs: severe COVID-19
- Any unsolicited AESIs: PIMMCs
- Any unsolicited AESIs: NOCMs
- Any unsolicited AESIs: Serologically or Virologically Events Confirmed Relevant to COVID-19
- Any Treatment-Related AEs
- Any Treatment-Related MAAEs
- Any Treatment-Related unsolicited AESIs: severe COVID-19
- Any Treatment-Related AESIs: PIMMCs
- Any Treatment-Related AESIs: NOCMs
- Any Treatment-Related unsolicited AESIs: Serologically or Virologically Events Confirmed Relevant to COVID-19

All the categories above will be summarized by SOC and PT separately.

In addition, separate listings containing individual subject adverse event data for unsolicited AEs, unsolicited TEAEs leading to discontinuati n from participation in the study or study treatment, serious AEs and unsolicited MAAEs will be provided separately.

9.1.1.1. Relationship of Adverse Events to Study Drug

For each reported adverse reaction, the participating site's PI or qualified designee must assess the relationship of the event to GRT-R910 using the following guidelines:

- Related – The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE.
- Not Related – There is not a reasonable possibility that the administration of the study product caused the event, there is no temporal relationship between the study product and event onset, or an alternate etiology has been established.

All TEAEs will be presented in a summary table for each treatment group and total by SOC, PT, and relationship to study vaccine. A separate summary will be provided for TEAEs through 28 days after GRT-R910 vaccination. If a subject has 2 or more TEAEs in the same SOC (or with the same PT) with a different relationship to study vaccine, then the subject will be counted under "Related". If the relationship information is missing, the AE will be considered related in the summary but will be presented as missing in the data listings.

9.1.1.2. Severity of Adverse Event

All AEs or SAEs will be assessed for severity, according to the toxicity grading scales in the US Food and Drug Administration (FDA) guidance document entitled "Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials."

For AEs not included in the protocol-defined grading system, the following guidelines will be used to describe severity. The following grades will be used in this study:

- Mild (Grade 1): Events that are usually transient and may require only minimal or no treatment or therapeutic intervention and generally do not interfere with the subject's usual activities of daily living.
- Moderate (Grade 2): Events that are usually alleviated with additional therapeutic intervention. The event interferes with usual activities of daily living, causing discomfort but poses no significant or permanent risk of harm to the research subject.
- Severe (Grade 3): Events interrupt usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention. Severe events are usually incapacitating.
- Potentially Life-Threatening (Grade 4): Potentially Life-threatening refers to an AE that at occurrence represents an immediate risk of death to a subject. An event that may cause death if it occurs in a more severe form is not considered life-threatening.

All TEAEs and treatment-related TEAEs will be summarized for each treatment group and total by maximum severity, SOC, and PT. A separate summary will be provided for TEAEs through 28 days after GRT-R910 vaccination; th s includes the prime dose and booster vaccination. If a subject has more than one AE on the same level (e.g., SOC or PT), the most severe AE will be summarized. If the severity information is missing, the AE will be considered Potentially Life-Threatening in the summary but will be presented as missing in the data listings.

9.1.1.3. Serious Adverse Events

An SAE will be defined as any event that includes the following outcomes:

- Death
- A life-threatening AE
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

All SAEs will be recorded on the appropriate SAE DCF, will be followed through resolution or stabilization by a study clinician, and will be recorded through the end of study (EOS).

Suspected Unexpected Serious Adverse Reaction (SUSAR) will be recorded during the study. A SUSAR is any SAE where a causal relationship with the study product is at least reasonably possible but is not listed in the Investigator's Brochure (IB), Package Insert, and/or Summary of Product Characteristics.

9.1.1.4. Adverse Events of Special Interest (AESI)

For this study, protocol specified AESIs are serologically or virologically confirmed SARS-CoV-2 infection or severe COVID-19. AESIs also include the Brighton Collaboration AESIs relevant to vaccination that are listed below:

- NOCMCs – defined as any new ICD diagnosis (per current International Statistical Classification of Diseases and Related Health Problems) that is applied to the subject during the course of the study, after receipt of the study agent, that is expected to continue for at least 3 months and requires continued health care intervention.
- MAAEs – defined as hospitalization, an emergency room visit or an otherwise unscheduled visit to or from medical personnel for any reason.
- PIMMCs – These constitute a group of AEs that includes diseases which are clearly autoimmune in etiology and other inflammatory and/or neurologic disorders which may or may not have autoimmune etiology. PIMMCs that are of special interest for this study are Brighton Collaboration AESIs relevant to vaccination that include: seizures, Guillain-Barre syndrome, acute disseminated encephalomyelitis, vasculitis, anaphylaxis, vaccine associated enhanced respiratory disease, thrombocytopenia, and thrombotic events.

All AESIs will be assessed, recorded, and followed as described above under AEs.

AESIs that meet SAE crite ia will be reported on a SAE form within 24 hours of the site's awareness to the Gritstone/PPD Pharmacovigilance Group. In addition, for documentation and medical assessment purposes, AESIs that do not meet SAE criteria will also be reported on an SAE form within the period for AE reporting to the Gritstone/PPD Pharmacovigilance Group; however, the narrative will indicate that the AESI did not meet SAE criteria.

9.1.1.5. Adverse Events Leading to Vaccine Dose Delay

All AEs leading to vaccine dose delay will be presented in a data listing and in general summary tables.

9.1.1.6. Adverse Events Leading to Study Discontinuation

All AEs leading to study discontinuation will be presented in a data listing and in general summary tables.

9.1.1.7. Adverse Events Leading to Study Treatment Discontinuation

All AEs leading to study treatment discontinuation will be presented in a data listing and in general summary tables.

9.1.1.8. Fatal Adverse Events

Fatal adverse events are those adverse events (also SAEs) that lead to Death according to CRF data. Fatal AEs will be presented in a data listing and in general summary tables.

9.1.2. Solicited Adverse Events

Solicited AEs are anticipated local and systemic AEs for which consistent collection of information is desired. Study clinicians will follow and collect resolution information for any reactogenicity symptoms that are not resolved within 7 days post GRT-R910 vaccination (day of vaccination and 7 subsequent days).

Solicited AEs (i.e., reactogenicity) will be collected using a memory aid and recorded on the appropriate DCF from the time of GRT-R910 vaccination within 7 days after each GRT-R910 vaccination.

For this study, solicited AEs will be:

- Injection site pain
- Injection site tenderness
- Injection site erythema
- Injection site edema/induration
- Headache
- Fatigue
- Malaise
- Myalgia
- Arthralgia
- Nausea
- Chills
- Fever

The toxicity grade for fever will be derived from temperature per FDA guidance [7]:

Vital Signs	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Fever (°C) (°F)	38.0 – 38.4 100.4 – 101.1	38.5 – 38.9 101.2 – 102.0	39.0 – 40 102.1 – 104	> 40 > 104

Temperatures will be recorded by oral thermometer and only the highest temperature will be recorded.

Reactogenicity local reactions including erythema, induration/edema, pain, and tenderness.

Reactogenicity systemic reactions including fever, chills, fatigue, malaise, myalgia, arthralgia, headache, and nausea.

Reactogenicity reactions that cannot be classified in any of the aforementioned categories for local and systemic events will be reported and summarized as unsolicited adverse events, and presented in a separate listing.

Any serious reactogenicity will be reported and summarized as serious unsolicited adverse event (SAE) (section 9.1.1.3).

The number and percentage (with 95% Clopper-Pearson CIs [6]) of participants who reported any solicited AE on the vaccination day and through the 7 subsequent days (see the exact windows for each cohort in Table 5) will be tabulated by grade and treatment group for each vaccination. Percentages will be based upon the number of participants in the Safety Analysis Set within each vaccination group. Subjects will be counted once for the most severe event in cases where the subject reported more than one event per solicited AE category (e.g., injection site pain). In addition, the duration (in days) of solicited AEs after each vaccination will be summarized by treatment group for each vaccination. Duration will be calculated as the number of days of the Solicited AE during the special window (Table 5).

Table 5 Windows for solicited AEs per Cohort

Cohort	Vaccination Day	Windows for Solicited AEs
1 and 2 (Subjects NOT RECEIVING booster dose)	Day 1	Day 1 through Day 8
1 and 2 (Subjects RECEIVING booster dose)	Day 1	Day 1 through Day 8
	Day 113	Day 113 through Day 120
3, 4, and 6	Day 1	Day 1 through Day 8
	Day 29	Day 29 through Day 36

All solicited local and systemic AEs will be presented in the data listings, including a listing of solicited AEs.

Calculation of Solicited AEs duration

The number of days will be calculated at the level of subject, vaccination (prime or booster), and symptom as the longest duration of consecutive days after the injection (including the day of injection) the subjects' reported solicited AE occurs with a toxicity grade > 0. If the solicited AE continues beyond 8 days, the days from the solicited AE reported after 8 days will be included (e.g., an event that lasted 5 days in the first 8 days post injection and 4 days beyond 8 days post injection, the duration will be reported as >8 days). A separate example below illustrates how solicited AE duration is calculated:

Subject ID	Prime/Booster	Symptom	Timepoint	Severity	Grade
G0910000999	DOSE 1	Headache	Day 1	MILD	1
G0910000999	DOSE 1	Headache	Day 2	MILD	1
G0910000999	DOSE 1	Headache	Day 3	NONE	0
G0910000999	DOSE 1	Headache	Day 4	NONE	0
G0910000999	DOSE 1	Headache	Day 5	MILD	1

G0910000999	DOSE 1	Headache	Day 6	MODERATE	2
G0910000999	DOSE 1	Headache	Day 7	MODERATE	2
G0910000999	DOSE 1	Headache	Day 8	MILD	1
G0910000999	DOSE 1	Headache	Day 9	MILD	1
G0910000999	DOSE 1	Headache	Day 10	NONE	0

In the above example, the duration of the headache for the subject at dose 1 (prime dose) is 5 days. Note that there are two solicited AE episodes reported:

1. Starting Day 1 and ending Day 2 (2 days)
2. Starting Day 5 and ending Day 9 (5 days)

Only the length of the longest duration (the second episode) is considered, while the first episode is not. Each duration of episode is calculated via the formula:

$$Duration(days) = (end\ date\ of\ Solicited\ AE\ recorded\ in\ Memory\ Aid) - (start\ date\ of\ Solicited\ AE\ recorded\ in\ Memory\ Aid) + 1$$

9.1.3. Study Halting Rules

Section 11.6 of the protocol provides criteria that would trigger an immediate halt to dosing for all subjects until an assessment by the study team has taken place, and an amendment is submitted to, and approved by, the competent authority. Both solicited and unsolicited adverse events, and which (if any) study halting criteria they meet, are collected on the Study Halting Rule CRF, and will be presented in a data listing.

9.2. Clinical Laboratory Evaluations

The following tests will be performed by the local laboratory:

- Hematology:
  - White Blood Cells (WBC) Count
  - Hemoglobin (Hb)
  - Platelets (PLT)
  - Absolute Neutrophils
  - Absolute Lymphocytes
  - Absolute Monocytes
  - Absolute Eosinophils
  - Absolute Basophils
- Chemistry:
  - Alkaline phosphatase (ALP)

  - Alanine aminotransferase (ALT)
  - Aspartate aminotransferase (AST)
  - Total bilirubin
  - Creatine kinase (C)
  - Serum creatinine
- Coagulation:
  - Prothrombin Time (PT)/INR
  - Activated Partial Thromboplastin Time (aPTT)
- Serology:
  - HIV
  - Hepatitis B Surface Antigen (HbsAg)
  - Hepatitis C Antibody (HCV Ab)
  - SARS-CoV-2 serology (N-specific)

Serum or urine pregnancy test - Cohort 6 only: women of childbearing potential must have a negative urine or serum pregnancy test at screening for eligibility purposes and within 24 hours prior to each study vaccination. No tables but a listing will be provided for the test. Clinical safety laboratory parameters evaluated after receipt of GRT-R910 will include WBC, Hb, PLT, ALT, AST, ALP, total bilirubin, CK, and creatinine.

Actual results and changes from baseline values for hematology and serum chemistry tests will be summarized by study days and treatment group for scheduled visits only.

A summary of toxicity grades (from 0 t 4 where 0 is Normal result (not included in the other grades), 1 is Mild, 2 is Moderate, 3 is Severe, 4 is Potentially Life-threatening) will be reported by study days and treatment group using the frequency count and percentage of subjects in each category. Toxicity grading will be performed according to FDA guidance for healthy subjects [7].For chemistry and hematology parameters, shift in toxicity grades from baseline will be summarized by study days and t eatment group using the frequency count and percentage of subjects in each category. The shift in toxicity grades will be from baseline to the worst-case post-vaccination, which will include unscheduled and repeated assessments, will also be presented. If the toxicity grade is missing for an existing lab value, then it will not be imputed, and the result will be summarized in the "Grade Missing" category. Missing grades will not be included in the overall denominator of toxicity grade summaries.

Subjects will be screened for HIV, hepatitis B surface antigen, antibody to hepatitis C virus and SARS-CoV-2. Results will be discussed with the subject. If a positive result occurs, the subject will be referred for appropriate follow-up and results will be reported as required by state law. These screening tests must be negative for the subject to be eligible to participate. Serology data will not be summarized.

For subject with Early Termination (ET) visit, the ET visit will be set to the next protocol scheduled visit following ET within the specific study period. If the subjects completed all the scheduled visits and then discontinued, no mapping will be done. The worst-case toxicity grades post-vaccination, which will include unscheduled assessments, will also be presented.

All laboratory data will be presented in a data listing.

9.3. Vital Sign Measurements

Actual values and changes from baseline for vital sign data (oral temperature, systolic and diastolic blood pressure, and pulse rate) will be summarized by study days and treatment for subjects in the Safety Analysis Set. Changes from baseline to each scheduled post-baseline visit will be presented.

A summary of toxicity grades (from 0 to 4 where 0 is Normal result (not included in the other grades), 1 is Mild, 2 is Moderate, 3 is Severe, and 4 is Life-threatening or disabling [Subjects will only have temperature up to grade 4]) will be reported by study days and treatment group using the frequency count and percentage of subjects in each category (for more information see the "Guidance for Industry: Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials" [7]). Shift in toxicity grades from baseline will be summarized by study days and treatment group using the frequency count and percentage of subjects in each category. The shift in toxicity grades will be from baseline to the worst-case post-vaccination, which will include unscheduled and repeated assessments, will also be presented. Missing grades will be displayed as counts, but will not be included in the overall denominator of toxicity grade summaries.

All vital sign measurements will be presented in a data listing.

9.4. Cardiac biomarker

Cardiac biomarker assessment will be performed for Cohort 1 and 2 receiving booster dose only, and Cohort 3, 4, and 6.

Cardiac biomarker assessments include troponin T (cTnT), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). The biomarker assessments will be summarized as mean, SD, median, min, max, and mean of actual value and as mean, SD, median, min, and max of change from baseline. An interpretation by study days table will be summarized for the SAF.

For subject with Early Termination (ET) visit, the ET visit will be set to the next protocol scheduled visit following ET within the specific study period. If the subjects completed all the scheduled visits and then discontinued, no mapping will be done.

All data will also be presented in a data listing for SAF.

9.5. Physical Examination

Screening physical examination results will be reported via table and data listing, with below assessments captured:

- Height/Weight/BMI
- Skin
- Head, Eyes, Ears, Nose, Throat
- Respiratory

- Gastrointestinal
- Endocrine Metabolic
- Genitourinary
- Neurological
- Blood Lymphatic
- Musculoskeletal
- Other

A listing for post screening targeted physical examination with clinically abnormal result will be provided.

9.6. Electrocardiogram

Electrocardiogram (ECG) will be performed for Cohort 1 and 2 receiving booster dose only and Cohort 3, 4, and 6.

The ECG data will include heart rate and RR, PR, QT, and QRS durations. The investigator will be responsible for providing the interpretation of clinical significance for all ECG results.

The ECG assessments will be summarized as mean, SD, median, min, max, and mean of actual value and as mean, SD, median, min, and max of change from baseline. An interpretation by study days table in ECG will be summarized for the SAF

For subject with Early Termination (ET) visit, the ET visit will be set to the next protocol scheduled visit following ET within the specific study period. If the subjects completed all the scheduled visits and then discontinued, no mapping will be done.

All the ECG data will be listed.

10. Interim Analysis

No interim analysis was planned for this study; however, there may be unplanned interim analyses in light of the nature of Phase 1 study.

11. Changes in the Planned Analysis

- Efficacy analysis was added to the section 8.1
- Explained the occurrence of potential unplanned interim analyses in section 10.
- Calculation of solicited AE duration in section 9.1.2

12. References

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2. Gritstone bio, Inc. Clinical study protocol GO-009 Version 5.0 09 Feb 2023.
3. https://www.sas.com/en_us/home.html
4. Martin Bland Prof. of Health Statistics University of York, Detecting a single event

5. ICH. Guidance for Industry (Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2))
6. Clopper, C.J., and Pearson, E.S. (1934), "The Use of Confidence or Fiducial Limits Illustrated in the Case of the Binomial", Biometrika 26, 404-413
7. U.S. Department of Health and Human Services Food and Drug Administration Center for Biologics Evaluation and Research, "Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials", 2007

13. Appendices

Appendix 1

Table 6 Schedule of Study Procedures: Cohorts 1 and 2 – Subjects NOT receiving booster dose

Study Visit	V00	V01	V02	V03	V04	V05	V06	V07	V08	Unsch Visit	Early Term Visit
Study Day(s)	SCR -30 to -1	Day 1	Day 2 +1d	Day 4 +2d	Day 8 +2d	Day 29 ±3d	Day 57 ±3d	Day 180 ±3d	Day 365 ±7d		
Obtain Written Informed Consent	X										
Review Eligibility Criteria	X	X									
Medical History	X										
Review of Interim Medical History		X	X	X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X
Vital Signs (Oral Temp, Pulse, BP)	X	X			X	X	X	X	X	X	X
Physical Examination including Height and Weight	X										
Targeted Physical Examination, if indicated		X			X	X	X	X	X	X	X
Nasal Swab Collection for SARS-CoV-2 PCR	X									X[7]	
Blood Collection for Safety Labs	X[1]				X[2]		X[2]	X[2]		X[2]	X[2]
Blood Collection for HBsAg, Anti-HCV, SARS-CoV-2 serology[3], HIV	X						X[3]				
Blood Collection for Cellular Immune Assays		X			X	X		X	X	X	X
Blood Collection for Antibody Assays		X				X	X	X	X	X	X
Vaccination		X									
45 Minute Evaluation After Study Vaccination		X									
Distribute Memory Aid and Study-Related Materials		X									
Review Memory Aid			X	X	X					X[4]	X[4]

Study Visit	V00	V01	V02	V03	V04	V05	V06	V07	V08	Unsch Visit	Early Term Visit
Study Day(s)	SCR -30 to -1	Day 1	Day 2 +1d	Day 4 +2d	Day 8 +2d	Day 29 ±3d	Day 57 ±3d	Day 180 ±3d	Day 365 ±7d		
Adverse Events		X	X	X	X	X				X[5]	X[5]
SAEs/AESIs including PIMMCs/MAAEs/NOCMCs[8]		X[9]	X	X	X	X	X	X	X	X	X
Phone Visit[6]			X	X							
Saliva Collection for Antibodies		X			X			X			

Abbreviations: AESI, adverse event of special interest; BP, blood pressure; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus; MAAE, Medically Attended Adverse Event; NOCMC, New Onset Chronic Medical Condition; SAE, serious adverse event; PCR, polymerase chain reaction; PIMMC, Potentially Immune-Mediated Medical Condition; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SCR, screening; Unsch, unscheduled

1 Includes white blood cells (WBCs), hemoglobin (Hb), platelets (PLT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, creatine kinase (CK), serum creatinine, prothrombin time (PT)/international normalized ratio (INR), and activated partial thromboplastin time (aPTT)
2 Includes WBCs, Hb, PLT, ALT, AST, ALP, total bilirubin, CK, and serum creatinine
3 Includes SARS-CoV-2 serology (N-specific) only
4 If within 7 days after vaccination
5 If prior to Visit 05
6 Can be phone, text, or e-mail contact
7 A nasal swab for SARS-CoV-2 should be performed within 3 days of COVID-19 symptoms and repeated after 7 days.
8 AESIs, including serologically or virologically confirmed SARS-CoV-2 infection and severity of COVID-19, PIMMCs, MAAEs, and NOCMCs will be collected from the time of first vaccination throughout the entire study.
9 SAEs occurring after signing of the informed consent form (ICF) will be recorded and reported to the sponsor or designee by the investigator within 24 hours of becoming aware of the SAE.

Table 7 Schedule of Study Procedures: Cohorts 1 and 2 – Subjects receiving booster dose

Study Visit	V00	V01	V02	V03	V04	V05	V06	V07	V08	V09	V10	V11	V12	V13	V14	Unsch Visit	Early Term Visit
Study Day(s)	SCR -30 to -1	Day 1	Day 2 +1d	Day 4 +2d	Day 8 +2d	Day 29 ±3d	Day 57 ±3d	Day 113[12] -3d/+21d	Day 114 +1d	Day 116 +2d	Day 120 +2d	Day 142 ±3d	Day 170 ±3d	Day 293 ±3d	Day 478 ±7d		
Obtain Written Informed Consent	X																
Review Eligibility Criteria	X	X						X									
Medical History	X																
Review of Interim Medical History		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs (Oral Temp, Pulse, BP)	X	X			X	X	X	X			X	X	X	X	X	X	X
Physical Examination including Height and Weight	X																
Targeted Physical Examination, if indicated		X			X	X	X	X			X	X	X	X	X	X	X
ECG[8]		X[9]			X	X	X	X[9]			X	X	X	X	X		
Cardiac Biomarkers (Troponin T, CRP, ESR)[10]		X[11]			X	X	X	X[11]			X	X	X	X	X		
Nasal Swab Collection for SARS-CoV-2 PCR	X															X[7]	
Blood Collection for Safety Labs	X[1]				X[2]		X[2]				X[2]		X[2]	X[2]		X[2]	X[2]
Blood Collection for HBsAg, Anti-HCV, SARS-CoV-2 serology[3], HIV	X						X[3]						X[3]				

Study Visit	V00	V01	V02	V03	V04	V05	V06	V07	V08	V09	V10	V11	V12	V13	V14	Unsch Visit	Early Term Visit
Study Day(s)	SCR -30 to -1	Day 1	Day 2 +1d	Day 4 +2d	Day 8 +2d	Day 29 ±3d	Day 57 ±3d	Day 113[12] -3d/+21d	Day 114 +1d	Day 116 +2d	Day 120 +2d	Day 142 ±3d	Day 170 ±3d	Day 293 ±3d	Day 478 ±7d		
Blood Collection for Cellular Immune Assays		X			X	X		X				X		X	X	X	X
Blood Collection for Antibody Assays		X				X	X	X				X		X	X	X	X
Vaccination		X						X									
45 Minute Evaluation After Study Vaccination		X						X									
Distribute Memory Aid and Study-Related Materials		X						X									
Review Memory Aid			X	X	X				X	X	X					X[4]	X[4]
Adverse Events		X	X	X	X	X		X	X	X	X	X				X[5]	X[5]
SAEs/AESIs including PIMMCs/MAAEs/NOCMCs[13]	X[14]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Phone Visit[6]			X	X					X	X							
Saliva Collection for Antibodies		X			X			X			X			X			

Abbreviations: AESI, adverse event of special interest; BP, blood pressure; d, day(s); ECG, electrocardiogram; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus; MAAE, Medically Attended Adverse Event; NOCMC, New Onset Chronic Medical Condition; SAE, serious adverse event; PCR, polymerase chain reaction; PIMMC, Potentially Immune-Mediated Medical Condition; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SCR, screening; Unsch, unscheduled

1 Includes white blood cells (WBCs), hemoglobin (Hb), platelets (PLT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, creatine kinase (CK), serum creatinine, prothrombin time (PT)/international normalized ratio (INR), and activated partial thromboplastin time (aPTT)
2 Includes WBC, Hb, PLT, ALT, AST, ALP, total bilirubin, CK, and creatinine
3 Includes SARS-CoV-2 serology (N-specific) only
4 If within 7 days after each vaccination (prime or boost dose)
5 If prior to Visit 11

6 Can be phone, text, or e-mail contact
7 A nasal swab for SARS-CoV-2 should be performed within 3 days of COVID-19 symptoms and repeated after 7 days.
8 ECG will be performed for subjects receiving booster dose in Cohorts 1 and 2. ECG data will include heart rate and RR, PR, QT, and QRS durations.
9 ECG will be performed before 1st and 2nd doses of vaccination.
10 Cardiac biomarker assessment will be performed for subjects receiving booster dose in Cohorts 1 and 2. Cardiac biomarker assessments will include troponin T, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR).
11 Cardiac biomarker assessment will be performed before 1st and 2nd doses of vaccination.
12 In case of second dose delay (allowed -3 days/+21 days), all safety visits (Visit 08 to Visit 12) will be scheduled based on the day of the second dose (e.g., Visit 08 will occur 1 day after delayed second dose and not on Day 114). All visits will shift based on the second dose without changing the time interval between 2 consecutive visits.
13 AESIs, including serologically or virologically confirmed SARS-CoV-2 infection and severity of COVID-19, PIMMCs, MAAEs, and NOCMCs will be collected from the time of first vaccination throughout the entire study.
14 SAEs occurring after signing of the informed consent form (ICF) will be recorded and reported to the sponsor or designee by the investigator within 24 hours of becoming aware of the SAE.

Table 8 Schedule of Study Procedures: Cohorts 3, 4, and 6

Study Visit	V00	V01	V02	V03	V04	V05	V06	V07	V08	V09	V10	V11	V12	V13	Unsch Visit	Early Term Visit
Study Day(s)	SCR -30 to -1	Day 1	Day 2 +1d	Day 4 +2d	Day 8 +2d	Day 15 ±2d	Day 29 ±3d	Day 30 +1d	Day 32 +2d	Day 37 +2d	Day 58 ±3d	Day 86 ±3d	Day 209 ±3d	Day 394[16] ±7d		
Obtain Written Informed Consent	X															
Review Eligibility Criteria	X	X					X									
Medical History	X															
Review of Interim Medical History		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs (Oral Temp, Pulse, BP)	X	X			X	X	X			X	X	X	X	X	X	X
Physical Examination Including Height and Weight	X															
Targeted Physical Examination, if Indicated		X			X		X			X	X	X	X	X	X	X
ECG[8]		X[9]			X		X[9]			X	X	X	X	X		
Cardiac Biomarkers (Troponin T, CRP, ESR)[10]		X[11]			X		X[11]			X	X	X	X	X		
Nasal Swab Collection for SARS-CoV-2 PCR	X														X[7]	
Blood Collection for Safety Labs	X[1]				X[2]		X			X[2]		X[2]	X[2]		X[2]	X[2]
Blood Collection for HBsAg, Anti-HCV, SARS-CoV-2 Serology[3], HIV	X											X[3]				
Blood Collection for Cellular Immune Assays		X			X		X				X		X	X	X	
Blood Collection for Antibody Assays		X				X	X				X	X	X	X	X	X
Pregnancy Test (Women of Childbearing Potential)	X[12]	X[12]					X[12]									

Study Visit	V00	V01	V02	V03	V04	V05	V06	V07	V08	V09	V10	V11	V12	V13	Unsch Visit	Early Term Visit
Study Day(s)	SCR -30 to -1	Day 1	Day 2 +1d	Day 4 +2d	Day 8 +2d	Day 15 ±2d	Day 29 ±3d	Day 30 +1d	Day 32 +2d	Day 37 +2d	Day 58 ±3d	Day 86 ±3d	Day 209 ±3d	Day 394[16] ±7d		
Vaccination		X					X									
45 Minute Evaluation After Study Vaccination		X					X									
Distribute Memory Aid and Study-Related Materials		X					X									
Review Memory Aid			X	X	X			X	X	X					X[4]	X[4]
Adverse Events		X	X	X	X	X	X	X	X	X	X				X[5]	X[5]
SAEs/AESIs Including PIMMCs/MAAEs/NOCMCs[13]	X[14]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Phone Visit[6]			X	X				X	X							
Saliva Collection for Antibodies		X			X	X	X			X			X			

Abbreviations: AESI, adverse event of special interest; BP, blood pressure; ECG, electrocardiogram; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus; MAAE, Medically Attended Adverse Event; NOCMC, New Onset Chronic Medical Condition; SAE, serious adverse event; PCR, polymerase chain reaction; PIMMC, Potentially Immune-Mediated Medical Condition; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SCR, screening; Unsch, unscheduled

1 Includes white blood cells (WBCs), hemoglobin (Hb), platelets (PLT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, creatine kinase (CK), serum creatinine, prothrombin time (PT)/international normalized ratio (INR), and activated partial thromboplastin time (aPTT)
2 Includes WBC, Hb, PLT, ALT, AST, ALP, total bilirubin, CK, and creatinine
3 Includes SARS-CoV-2 serology (N-specific) only
4 If within 7 days after each vaccination (prime or boost dose)
5 If prior to Visit 10
6 Can be phone, text, or e-mail contact
7 A nasal swab for SARS-CoV-2 should be performed within 3 days of COVID-19 symptoms and repeated after 7 days.
8 ECG data will include heart rate and RR, PR, QT, and QRS durations.
9 ECG will be performed up to 72 hours before the 1st and up to 72 hours before the 2nd study vaccinations.
10 Cardiac biomarker assessments will include troponin T, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR).
11 Cardiac biomarker assessment will be performed before 1st and 2nd doses of vaccination.
12 Cohort 6 only: women of childbearing potential must have a negative urine or serum pregnancy test at screening for eligibility purposes and within 24 hours prior to each study vaccination.

13 AESIs, including serologically or virologically confirmed SARS-CoV-2 infection and severity of COVID-19, PIMMCs, MAAEs, and NOCMCs will be collected from the time of first vaccination throughout the entire study.
14 SAEs occurring after signing of the informed consent form (ICF) will be recorded and reported to the sponsor or designee by the investigator within 24 hours of becoming aware of the SAE.
15 In case of second dose delay (±3), all safety visits (Visit 07 to Visit 12) will be scheduled based on the day of the second dose (e.g., Visit 07 will occur 1 day after delayed second dose and not on Day 30). All visits will shift based on the second dose without changing the time interval between 2 consecutive visits.
16 Cohorts 3 and 4 will complete Visit 13 (Day 394) if the visit window occurs prior to the last study participant completing Visit 12 (Day 209). Cohort 6 will not complete Visit 13 (Day 394).

Appendix 2

Table 9 Planned Tables, Listings, and Figures (TLFs)

#	Type	Output #	Output Header	Population
1	Table	14.1.1.1	Subject Screening and Enrollment	All Screened Subjects Analysis Set
2	Table	14.1.1.2	Subjects Disposition and Analysis Sets	Intent-to-Treat Analysis Set*
3	Table	14.1.2.2	Major Protocol Deviations	Safety Analysis Set
4	Table	14.1.3	Demographics	Safety Analysis Set
5	Table	14.1.4	Medical History	Safety Analysis Set
6	Table	14.2.1	Analysis of Incidence Rate of COVID-19 Positive Tests	Safety Analysis Set
7	Table	14.3.1.1.1	Summary of Subjects with Solicited Adverse Events Within 8 Days After the Injection of Prime Dose by Maximum Grade	Safety Analysis Set
8	Table	14.3.1.1.2	Summary of Subjects with Solicited Adverse Events W thin 8 Days After the Injection of Booster Dose by Maximum Grade	Safety Analysis Set
9	Table	14.3.1.2.1	Summary of Subjects with Solicited Adverse Events Within 8 Days After the Injection of Prime Dose by Maximum Grade and Onset Day	Safety Analysis Set
10	Table	14.3.1.2.2	Summary of Subjects with Solicited Adverse Events Within 8 Days After the Injection of Booster Dose by Maximum Grade and Onset Day	Safety Analysis Set
11	Table	14.3.1.3.1	Summary of Subjects with Solicited Adverse Events Within 8 Days After the Injection of Prime Dose by Onset Day	Safety Analysis Set
12	Table	14.3.1.3.2	Summary of Subjects with Solicited Adverse Events Within 8 Days After the Injection of Booster Dose by Onset Day	Safety Analysis Set

13	Table	14.3.1.4.1	Subject Incidence of Solicited Adverse Events by Term Related to the Injection of Prime Dose	Safety Analysis Set
14	Table	14.3.1.4.2	Subject Incidence of Solicited Adverse Events by Term Related to the Injection of Booster Dose	Safety Analysis Set
15	Table	14.3.1.4.3	Summary of Duration (Days) of Solicited Adverse Events Related to the Injection of Prime Dose	Safety Analysis Set
16	Table	14.3.1.4.4	Summary of Duration (Days) of Solici ed Adverse Events Related to the Injection of Boost r Dose	Safety Analysis Set
17	Table	14.3.1.5.1	Summary of Subjects with Solicited Adverse Events Beyond 8 Days Related to the I jection of Prime Dose by Maximum Grad	Safety Analysis Set
18	Table	14.3.1.5.2	Summary of Subjects with Solicited Adverse Events Beyond 8 Days Related to the Injection of Booster Dose by Maximum Grade	Safety Analysis Set
19	Table	14.3.1.6.1	Summary of Unsolicited TEAEs Throughout the St dy	Safety Analysis Set
20	Table	14.3.1.7.1	Subject Incidence of Unsolicited TEAEs by Maximum Severity, System Organ Class and P eferred Term up to 28 Days After the Injection of Prime Dose	Safety Analysis Set
21	Table	14.3.1.7.2	Subject Incidence of Unsolicited TEAEs by Maximum Severity, System Organ Class and Preferred Term up to 28 Days After the Injection of Booster Dose	Safety Analysis Set
22	Table	14.3.1.8.1	Subject Incidence of Unsolicited TEAEs by System Organ Class and Preferred Term up to 28 Days After the Injection of Prime Dose	Safety Analysis Set

23	Table	14.3.1.8.2	Subject Incidence of Unsolicited TEAEs by System Organ Class and Preferred Term up to 28 Days After the Injection of Booster Dose	Safety Analysis Set
24	Table	14.3.1.9.1	Subject Incidence of Unsolicited Treatment-Related TEAEs by System Organ Class and Preferred Term up to 28 Days After the Injection of Prime Dose	Safety Analysis Set
25	Table	14.3.1.9.2	Subject Incidence of Unsolicited Treatment-Related TEAEs by System Organ Class and Preferred Term up to 28 Days After the Injection of Booster Dose	Safety Analysis Set
26	Table	14.3.1.10	Subject Incidence of Unsolic ted TEAEs by System Organ Class and Pref rred Term Throughout the Study	Safety Analysis Set
27	Table	14.3.1.11	Subject Inciden e of Unsolicited Treatment-Related TEAE by System Organ Class and Preferred Term Th oughout the Study	Safety Analysis Set
28	Table	14.3.1.12	Subj ct Incidence of Serious TEAEs by System Organ Class and Preferred Term Throughout the Study	Safety Analysis Set
29	Table	14.3.1.13	Subject Incidence of Serious Treatment-Related TEAEs by System Organ Class and Preferred Term Throughout the Study	Safety Analysis Set
30	Table	14.3.1.14.1	Subject Incidence of Unsolicited Severe TEAEs by System Organ Class and Preferred Term up to 28 Days After the Injection of Prime Dose	Safety Analysis Set
31	Table	14.3.1.14.2	Subject Incidence of Unsolicited Severe TEAEs by System Organ Class and Preferred Term up to 28 Days After the Injection of Booster Dose	Safety Analysis Set

32	Table	14.3.1.15.1	Subject Incidence of Unsolicited Severe Treatment-Related TEAEs by System Organ Class and Preferred Term up to 28 Days After the Injection of Prime Dose	Safety Analysis Set
33	Table	14.3.1.15.2	Subject Incidence of Unsolicited Severe Treatment-Related TEAEs by System Organ Class and Preferred Term up to 28 Days After the Injection of Booster Dose	Safety Analysis Set
34	Table	14.3.1.16	Summary of Unsolicited TEAEs of Sp cial Interest Throughout the Study	Safety Analysis Set
35	Table	14.3.1.17	Subject Incidence of Unsolicited TEAEs of Special Interest by System Organ Class nd Preferred Term Throughout the Study	Safety Analysis Set
36	Table	14.3.1.18	Subject Incidence of Unsolicited Treatment-Emergent MAAEs by System Organ Class and Preferred Term Through ut t e Study	Safety Analysis Set
37	Table	14.3.1.19	Subject Incidence of Unsolicited Treatment-Emergent Severe COVID-19 by System Organ Class and Preferred Term Throughout the Study	Safety Analysis Set
38	Table	14.3.1.20	Subject Incidence of Unsolicited Treatment-Emergent PIMMCs by System Organ Class and Preferred Term Throughout the Study	Safety Analysis Set
39	Table	14.3.1.21	Subject Incidence of Unsolicited Treatment-Emergent NOCMs by System Organ Class and Preferred Term Throughout the Study	Safety Analysis Set
40	Table	14.3.1.22	Subject Incidence of Unsolicited Treatment-Emergent Serologically or Virologically Events Confirmed Relevant to COVID-19 by System Organ Class and Preferred Term Throughout the Study	Safety Analysis Set

41	Table	14.3.1.23	Subject Incidence of Unsolicited Treatment-Related Treatment-Emergent MAAEs by System Organ Class and Preferred Term Throughout the Study	Safety Analysis Set
42	Table	14.3.1.24	Subject Incidence of Unsolicited Treatment-Related Treatment-Emergent PIMMCs by System Organ Class and Preferred Term Throughout the Study	Safety Analysis Set
43	Table	14.3.1.25	Subject Incidence of Unsolicited Treatment-Related Treatment-Emergent NOCMCs by System Organ Class and Preferred Term Throughout the Study	Safety Analysis Set
44	Table	14.3.4.1.1.1	Summary of Actu l Value and Change from Baseline in Hematology	Safety Analysis Set – Cohort 1 and 2 without Booster Dose
45	Table	14.3.4.1.1.2	Summary of Actual Value and Change from Baseline in H matology	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
46	Table	14.3.4.1.1.3	Summary of Actual Value and Change from Baseline in Hematology	Safety Analysis Set – Cohort 3, 4, and 6
47	Table	14.3.4.1.2.1	Summary of FDA Toxicity Grades for Hematology	Safety Analysis Set – Cohort 1 and 2 without Booster Dose
48	Table	14.3.4.1.2.2	Summary of FDA Toxicity Grades for Hematology	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
49	Table	14.3.4.1.2.3	Summary of FDA Toxicity Grades for Hematology	Safety Analysis Set – Cohort 3, 4, and 6
50	Table	14.3.4.1.3.1	Shift from Baseline in Toxicity Grades for Hematology	Safety Analysis Set – Cohort 1 and 2 without Booster Dose

51	Table	14.3.4.1.3.2	Shift from Baseline in Toxicity Grades for Hematology	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
52	Table	14.3.4.1.3.3	Shift from Baseline in Toxicity Grades for Hematology	Safety Analysis Set – Cohort 3, 4, and 6
53	Table	14.3.4.2.1.1	Summary of Actual Value and Change from Baseline in Chemistry	Safety Analysis Set – Cohort 1 and 2 without Booster Dose
54	Table	14.3.4.2.1.2	Summary of Actual Value and Change from Baseline in Chemistry	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
55	Table	14.3.4.2.1.3	Summary of Actual Value and Change from Baseline in Chemistry	Safety Analysis Set – Cohort 3, 4, and 6
56	Table	14.3.4.2.2.1	Summary of FDA Toxici y Grades for Chemistry	Safety Analysis Set – Cohort 1 and 2 without Booster Dose
57	Table	14.3.4.2.2.2	Summary f FDA Toxicity Grades for Chemistry	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
58	Table	14.3.4.2.2.3	Summary of FDA Toxicity Grades for Chemistry	Safety Analysis Set – Cohort 3, 4, and 6
59	Table	14.3.4.2.3.1	Shift from Baseline in Toxicity Grades for Chemistry	Safety Analysis Set – Cohort 1 and 2 without Booster Dose
60	Table	14.3.4.2.3.2	Shift from Baseline in Toxicity Grades for Chemistry	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
61	Table	14.3.4.2.3.3	Shift from Baseline in Toxicity Grades for Chemistry	Safety Analysis Set – Cohort 3, 4, and 6
62	Table	14.3.4.3.1.1	Summary of Actual Value and Change from Baseline in Coagulation	Safety Analysis Set – Cohort 1 and 2 without Booster Dose
63	Table	14.3.4.3.1.2	Summary of Actual Value and Change from Baseline in Coagulation	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
64	Table	14.3.4.3.1.3	Summary of Actual Value and Change from Baseline in Coagulation	Safety Analysis Set – Cohort 3, 4, and 6

65	Table	14.3.4.3.2.1	Summary of FDA Toxicity Grades for Coagulation	Safety Analysis Set – Cohort 1 and 2 without Booster Dose
66	Table	14.3.4.3.2.2	Summary of FDA Toxicity Grades for Coagulation	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
67	Table	14.3.4.3.2.3	Summary of FDA Toxicity Grades for Coagulation	Safety Analysis Set – Cohort 3, 4, and 6
68	Table	14.3.5.1.1	Summary of Actual Value and Change from Baseline in Vital Signs	Safety Analysis Set – Cohort 1 and 2 without Booster Dose
69	Table	14.3.5.1.2	Summary of Actual Value and Change fr m Baseline in Vital Signs	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
70	Table	14.3.5.1.3	Summary of Actual Value and Change from Baseline in Vital Signs	Safety Analysis Set – Cohort 3, 4, and 6
71	Table	14.3.5.2.1	Summary of FDA Toxicity Grades for Vital Signs	Safety Analysis Set – Cohort 1 and 2 without Booster Dose
72	Table	14.3.5.2.2	Summary of FDA Toxicity Grades for Vital Signs	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
73	Table	14.3.5.2.3	Summary of FDA Toxicity Grades for Vital Signs	Safety Analysis Set – Cohort 3, 4, and 6
74	Table	14.3.5.3.1	Shift from Baseline in Toxicity Grades for Vital Signs	Safety Analysis Set – Cohort 1 and 2 without Booster Dose
75	Table	14.3.5.3.2	Shift from Baseline in Toxicity Grades for Vital Signs	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
76	Table	14.3.5.3.3	Shift from Baseline in Toxicity Grades for Vital Signs	Safety Analysis Set – Cohort 3, 4, and 6
77	Table	14.3.5.4.1	Cardiac biomarker assessments Interpretation by Visit	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
78	Table	14.3.5.4.2	Cardiac biomarker assessments Interpretation by Visit	Safety Analysis Set – Cohort 3, 4, and 6

79	Table	14.3.5.4.3	Summary of Actual Value and Change from Baseline in Cardiac biomarker assessments	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
80	Table	14.3.5.4.4	Summary of Actual Value and Change from Baseline in Cardiac biomarker assessments	Safety Analysis Set – Cohort 3, 4, and 6
81	Table	14.3.5.5.1	Screening Physical Examination Results	Safety Analysis Set
82	Table	14.3.5.6.1	Electrocardiogram Interpretation by Visit	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
83	Table	14.3.5.6.2	Electrocardiogram Interpretation by Visit	Safety Analysis Set – Cohort 3, 4, and 6
84	Table	14.3.5.6.3	Change from Baseline in Electrocardiogram Results	Safety Analysis Set – Cohort 1 and 2 with Booster Dose
85	Table	14.3.5.6.4	Change from Baseline in Electrocardiogram Results	Safety Analysis Set – Cohort 3, 4, and 6
86	Table	14.4.1	Vaccina ion Administration	Safety Analysis Set
87	Table	14.4.2.1	Recent Vaccinations and Concomitant Medications	Safety Analysis Set
88	Listing	16.2.1.1	Screen Failures	All Screened Subjects Analysis Set
89	Listing	16.2.1.2	Subject Disposition	Intent-to-Treat Analysis Set*
90	Listing	16.2.2.1	Inclusion/Exclusion Criteria	All Screened Subjects Analysis Set
91	Listing	16.2.2.2	Protocol Deviations	Intent-to-Treat Analysis Set*
92	Listing	16.2.3	Analysis Sets	All Screened Subjects Analysis Set
93	Listing	16.2.4.1	Demographics	Safety Analysis Set
94	Listing	16.2.4.2	SARS-CoV-2 PCR	Safety Analysis Set
95	Listing	16.2.4.3	Medical or Surgical History	Safety Analysis Set
96	Listing	16.2.4.4	Recent Vaccinations or Concomitant Medications	Safety Analysis Set
97	Listing	16.2.5.1	Vaccination	Safety Analysis Set
98	Listing	16.2.7.1	Solicited Local Adverse Events	Safety Analysis Set
99	Listing	16.2.7.2	Solicited Systemic Adverse Events	Safety Analysis Set

100	Listing	16.2.7.3	Unsolicited TEAEs	Safety Analysis Set
101	Listing	16.2.7.4	Treatment-Related Unsolicited TEAEs	Safety Analysis Set
102	Listing	16.2.7.5	Serious TEAEs	Safety Analysis Set
103	Listing	16.2.7.6	Serious Treatment-Related TEAEs	Safety Analysis Set
104	Listing	16.2.7.7	Unsolicited TEAEs Leading to Vaccine Dose Delay	Safety Analysis Set
105	Listing	16.2.7.8	Unsolicited TEAEs Leading to Study Discontinuation	Safety Analysis Set
106	Listing	16.2.7.9	Unsolicited TEAEs Leading to Study Drug Discontinuation	Safety Analysis Set
107	Listing	16.2.7.10	Fatal TEAEs	Safety Analysis Set
108	Listing	16.2.7.11	Other Symptoms from Mem ry Aid	Safety Analysis Set
108	Listing	16.2.8.1	Laboratory Results - H matology	Safety Analysis Set
109	Listing	16.2.8.2	Laboratory Results Chemistry	Safety Analysis Set
110	Listing	16.2.8.3	Laboratory Res lts - Coagulation	Safety Analysis Set
111	Listing	16.2.8.4	Laborat ry Results - Serology	Safety Analysis Set
112	Listing	16.2.9.1	Vital Signs Results	Safety Analysis Set
113	Listing	16.2.9.2	Sc eening Physical Examination Results	Safety Analysis Set
114	Listing	16.2.9.3	Cardiac Biomarker Assessments	Safety Analysis Set
115	Listing	16.2.9.4	Electrocardiogram Results	Safety Analysis Set
116	Listing	16.2.9.5	Targeted Physical Examination Results	Safety Analysis Set
117	Listing	16.2.9.6	Laboratory Results – Pregnancy test	Safety Analysis Set – Cohort 6
118	Listing	16.2.10.1	Study Halting Rules	Safety Analysis Set

DocuSign

Certificate Of Completion

Envelope Id: [redacted]
Status: Completed
Subject: Complete with DocuSign: Gritstone_Bio_GRTGO009_SAPv5.0.pdf
Source Envelope:
Document Pages: 49
Signatures: 4
Certificate Pages: 3
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Disabled
Time Zone: (UTC) Monrovia, Reykjavik
Envelope Originator:
[redacted]

Record Tracking

Status: Original
08 June 2023 | 23:10
Holder: [redacted]
Location: DocuSign

Signer Events	Signature	Timestamp
[redacted] PPD 21 CFR Part 11 Security Level: Email, Account Authentication (Required)	[redacted] Signature Adoption: Pre-selected Style [redacted] With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this doc ment	Sent: 08 June 2023 | 23:20 Viewed: 09 June 2023 | 13:05 Signed: 09 June 2023 | 13:17
Electronic Record and Signature Disclosure: Not Offered via DocuSign		
[redacted] Gritstone bio, Inc. Security Level: Email, Account Authentication (Required)	[redacted] Signature Adoption: Pre-selected Style [redacted] With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 09 June 2023 | 13:17 Viewed: 12 June 2023 | 21:37 Signed: 12 June 2023 | 22:16
Electronic Record and Signature Disclosure: Accepted: 01 February 2023 | 16:56 [redacted]		

Signer Events	Signature	Timestamp
[redacted] Infectious Diseases Gritstone bio, Inc. Security Level: Email, Account Authentication (Required), Login with SSO	[redacted] Signature Adoption: Pre-selected Style [redacted] With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 12 June 2023 | 22:16 Resent: 20 June 2023 | 12:31 Viewed: 22 June 2023 | 15:35 Signed: 22 June 2023 | 15:36
Electronic Record and Signature Disclosure: Accepted: 16 March 2023 | 17:39 [redacted]		
[redacted] Security Level: Email, Account Authentication (Required)	[redacted] Signature Adoption: Drawn on Device [redacted] With Signing Authentication via DocuSign password With Signing Reasons (o ach tab): I am the author of th s document	Sent: 22 June 2023 | 15:36 Viewed: 22 June 2023 | 15:56 Signed: 22 June 2023 | 15:59
Electronic Record and Signature Disclosure: Not Offered via DocuSign		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	08 June 2023 | 23:20
Certified Delivered	Security Checked	22 June 2023 | 15:56
Signing Complete	Security Checked	22 June 2023 | 15:59
Completed	Security Checked	22 June 2023 | 15:59

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

PPD has established a corporate policy regarding the appropriate use of electronic records and electronic signatures, POL-00392, Appropriate Use of Electronic Records and Electronic Signatures