STATISTICAL ANALYSIS PLAN

Study Title

Multicenter, randomized, combined Phase I dose-escalation and Phase IIa double-blind, placebo-controlled study of the safety, tolerability, and immunogenicity of GLS-5310 DNA vaccine, administered intradermally against SARS-CoV-2 in healthy adults

Protocol No./Version

CoV2-001/5.0

Sponsor

GeneOne Life Science Inc.

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C&R Research

Signature Page

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Abbreviation

Term	Definition
ADR	Adverse Drug Reaction
AE	Adverse Events
ATC code	Anatomical Therapeutic Chemical code
CS	Clinically Significant
ID	Intradermal
ITT	Intention-To-Treat
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intention-To-Treat
NCS	Not Clinically Significant
PBMCs	Peripheral blood mononuclear cells
PPS	Per-Protocol Set
PRNT	Plaque reduction neutralization titer
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SARS-CoV	Severe acute respiratory syndrome coronavirus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus, type 2
SD	Supporting Documents
SOC	System Organ Class
SOP	Standard Operating Procedure
WHODD	WHO Drug Dictionary

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1. Study Objectives

1.1 Primary Objective – Phase I / IIa study

- Evaluate the safety and tolerability of GLS-5310 DNA vaccine
- Determine the binding antibody responses induced by GLS-5310 DNA vaccine relative to treatment arm

1.2 Secondary Objective – Phase I / IIa study

- Determine the T cell responses induced by GLS-5310 DNA vaccine
- Determine the neutralizing antibody response induced by GLS-5310

1.3 Exploratory Objective

Phase IIa Exploratory Objectives

- Determine the degree of immune response to GLS-5310 in participants under the age of 65 and those aged 66 to 85

2. Study Endpoints

2.1 Safety Endpoints

- Adverse Events (AEs)
- Vital signs
- Laboratory tests
- Assessment of Injection Site - The Solicited local AEs and Solicited Systemic AEs

2.2 Immunogenicity Endpoints

- Evaluation of GMT and serum conversion rates of SARS-CoV-2 Spike and ORF3a protein-specific binding antibodies induced by GLS-5310 (the end-point titer of binding antibodies in serum at each timepoint)
- Evaluation of GMT and positive responder rate of neutralizing antibody responses induced by GLS-5310 (plaque-reduction neutralizing titer, PRNT in serum at each timepoint)
- Evaluation of positive responder rate of T cell response induced by GLS-5310 (antigen-specific interferon – gamma (IFN-γ) secretion T-cell response in PBMC at each timepoint)

2.3 Exploratory Endpoints

2.3.1 Phase IIa Exploratory Endpoint

- Evaluation of the degree of immune response to GLS-5310 in subjects under 65 years of age and those aged 66 to 85 years of age

3. Study Design

The Phase I / IIa study aims to evaluate the safety, tolerability and immunogenicity of GLS-5310 DNA vaccine.

The Phase I study is an open-label, dose escalation study. The Phase I study will assess two different dose levels of GLS-5310, LOW DOSE (0.6mg) and HIGH DOSE (1.2mg); two different vaccination schemas with vaccinations given ID at either 0 and 8 weeks or 0 and 12 weeks. GLS-5310 will be administered via intradermal (ID) injection using the Mantoux technique followed by suction applied over the vaccination site using the JM-11 device.

The Phase IIa study is designed as randomized, double-blind, placebo-controlled and will assess a single vaccination regimen with corresponding dose level chosen from the Phase I study. Randomization between Vaccine and Placebo arms will be in a 2:1 ratio. The study will be unblinded at the post-vaccination visit (Visit 4) at which time subjects will be informed of their treatment assignment. Subjects who were assigned to the placebo group will be offered to be vaccinated with GLS-5310 and will be followed for a year from 1st GLS-5310 vaccination. However, subjects assigned to the placebo group but who decline vaccination with GLS-5310 will be followed for a year from study entry as per the original study protocol.

4. Planned Analysis

4.1 Interim Analysis

Interim analyses were performed in stages.

- **Stage 1:** An assessment of AE's was performed after study Visit 1 for Group 1a.
- **Stage 2:** When all Phase l subjects (Groups 1a, 1b and 1c) had completed Visit 4, an interim analysis was performed to evaluate safety and antibody response.

  In order for the study to move into Phase lla study, the seroconversion rate for the binding antibody responses must be >70%. In addition, the incidence of Serious Adverse Events (Grade 3 or higher) related to the investigational product should be no more than 1 case.
- **Stage 3:** An interim analysis of Phase lla study was performed after all patients complete their Visit 4. The purpose of this interim analysis was to provide options to placebo vaccinated subjects and to assess the safety of the vaccine after the second dose. For the interim analysis of Phase lla, database locking was implemented before unblinding.

The study is unblinded at the post-vaccination visit (study Visit 4) at which time subjects are informed of their treatment assignment. Subjects who were assigned to the placebo group are offered to be vaccinated with GLS-5310. Subjects assigned to the placebo group who choose to be vaccinated with GLS-5310 are followed for a year from 1st GLS-5310 vaccination; subjects assigned to the placebo group but who decline vaccination with GLS-

5310 are followed for a year from study entry as per the original study protocol.

5. Determination of Sample Size

This is an exploratory and descriptive Phase I/IIa clinical trial to evaluate the safety and immunogenicity of GLS-5310 for the purpose of preventing COVID-19, and dose not test statistical hypotheses, so the sample size is set within the limit of satisfying the research purpose. In the Phase I clinical trial, 45 subjects who meet the inclusion and exclusion criteria are registered to secure 15 subjects based on the allocation of each vaccination group. In the Phase IIa clinical trial, it is planned to secure 120 subjects based on randomization.

Randomization is performed 1:1 in 1b and 1c groups of Phase I clinical trial according to the planned random number, and 1:2 in placebo and vaccination groups in Phase IIa clinical trial to determine the difference between placebo and vaccination groups.

6. Analysis Sets

Safety and tolerability analyses will be performed on Safety Set.

- ✓ **Intention to treat (ITT)**
  Intention to treat (ITT) will include all participants who sign informed consent.

- ✓ **Modified Intention to treat (mITT)**
  Modified intention to treat (mITT) will include all participants who sign informed consent and who have received at least one administration of investigational product. The mITT will be the primary analysis population for baseline and demographic assessments and efficacy outcomes. All subjects will be summarized based on the treatment group to which they were assigned. Since not all subjects will have evaluable immune response data, analysis of immune responses will be performed only for available samples.

- ✓ **Safety Set (SS)**
  Safety Set (SS) will include all mITT participants. The SS will be the primary population for summary and analysis of safety assessments. All subjects will be summarized based on the treatments that actually received.

- ✓ **Per-Protocol Set (PPS)**
  Per-Protocol Set (PPS) will include all mITT participants who complete the trial by receiving all

vaccinations and have no significant protocol violations. This set will be used as a sensitivity analysis to summarize the primary and secondary response outcomes. For secondary and exploratory assessments of antibody and T cell immune responses, denominators will include only those participants who are SARS-CoV-2 seronegative at baseline. Unevaluable samples will not be considered as part of the denominator at relevant time points.

Protocol violations that can be excluded from the analysis group include the following and are defined according to the analysis population's definition of 'SOP 0406'.

- Participants who have never been vaccinated with all vaccinations
- Positive for SARS-CoV-2 serum test at Baseline
- Inclusion/Exclusion criteria violation
- Contraindicated drug administration
- Randomization errors
- Vaccination errors
- No blood draw for immunogenicity assessment

6.1 Errors in Investigational Product Vaccination

If a subject was not administered with the investigational product that was randomized (planned), the subject will be analyzed according to the following rule:

- If the wrong treatment was used for the entire trial, then he/she will be analyzed according to the actual treatment group for the safety analyses and randomized treatment group for the immunogenicity analyses complying to the intent-to-treat (ITT) principle.
- If the wrong treatment was use for only one of the vaccinations, he/she will be grouped into the highest dose (1.2 mg in Phase I, or treatment arm in Phase IIa) for safety and in the randomized arm for the immunogenicity analyses.

7. General Analysis Considerations

7.1 Statistical Analysis Software

Statistical analyses will be performed using a version 9.4 64bit (SAS Institute, Cary, NC, USA) or higher on the SAS® Enterprise Guide (version 8.2 and later) interface.

7.2 General Considerations

Descriptive statistics will be used to summarize the trial results. Continuous variables will be summarized with number of subjects, means, standard deviation (SD), median, minimum, and maximum. Categorical variables will be summarized with frequency and percentage. Unless particularly specified, all tests are based on a two-sided test at a significance level of 5%.

Values that contain decimals such as mean, SD, percentages, etc. will be at the same level as the raw data for medians, minimum and maximum, plus 1 decimal place for means, and plus 2 decimals for SD. All percentages will be presented to 1 decimal place.

Details will be included in listing sorted by phases and by groups.

7.3 Sub Analysis

A sub analysis about safety and immunogenicity is performed for under 65 years and 66-85 years of age.

8. Data Handling Conventions

8.1 Early Termination and Missing Data

In the event that dates and/or times are missing for medications, medications will be assumed to be concomitant. If only partial dates/times are missing and it is clear that medications were discontinued prior to study enrollment, medications will be assumed to be prior. In the event dates or times are missing for AEs, AEs will assume to be treatment emergent. Missing outcomes values, such as missed lab draws or invalid blood sample, missed vital signs, or missed or uninterpretable serum concentrations and PBMCs will be left as missing and not imputed. For the immunology analyses, statistical assessment will be based on available results.

In the event that a participant is enrolled in the trial but declines to be vaccinated, the site will enroll a replacement.

8.2 Handling of Missing Data

If there are missing dates and are used in calculations, they will be imputed as the following:

Table 1 Handling of missing or partial date

Types of Dates	Missing	Imputation	Examples
Prior/ Concomitant medication start date	YYYY-MM-DD	Year of the date of informed consent-01(January)-01	Date of informed consent: 2018-12-05 Collected date: UK-UK-UK Imputed date: 2018-01-01

Types of Dates	Missing	Imputation	Examples
	MM-DD	01(January)-01	Collected date: 2018-UK-UK Imputed date: 2018-01-01
	DD	01	Collected date: 2018-12-UK Imputed date: 2018-12-01
Prior/ Concomitant medication end date	YYYY-MM-DD	Final visit date	Final visit date: 2018-12-25 Collected date: UK-UK-UK Imputed date: 2018-12-25
	MM-DD	12-31	Collected date: 2018-UK-UK Imputed date: 2018-12-31
	DD	Last day of the month	Collected date: 2018-12-UK Imputed date: 2018-12-31
AE start date	YYYY-MM-DD	First IP administration date	Date of first IP administration: 2018-12-05 Collected date: UK-UK-UK Imputed date: 2018-12-05
	MM-DD	1. The year of the IP administration date = The year of the AE start date: The month and day of the IP administration date 2. The year of the IP administration date ≠ The year of the AE start date: 01-01	1. Date of IP administration: 2018-12-05 Collected date: 2018-UK-UK Imputed date: 2018-12-05 2. Date of IP administration: 2018-12-05 Collected date: 2019-UK-UK Imputed date: 2019-01-01
	DD	1. The year and the month of the IP administration date = The year and the month of the AE start date: The day of the IP administration date 2. The year and the month of the IP administration date ≠ The year and the month of the AE start date: 01	1. Date of IP administration: 2018-12-05 Collected date: 2018-12-UK Imputed date: 2018-12-05 2. Date of IP administration: 2018-12-05 Collected date: 2019-05-UK Imputed date: 2019-05-01
AE end date	YYYY-MM-DD	1. If the subject is dead: Death date 2. If the subject is not dead and has date of the last observation/date of early termination: Last observation/date of early termination	1. Death date: 2018-12-30 Collected date: UK-UK-UK Imputed date: 2018-12-30 2. Last observation/early termination date: 2018-12-30 Collected date: UK-UK-UK Imputed date: 2018-12-30

8.3 Analysis Visit Definition

Subjects who drop out after discontinuation of investigational product administration are required to perform a termination visit. If the termination visit date is included in the planned visit period and the corresponding visit result does not exist, the termination visit result is considered as the planned visit result and included in the

analysis. If the result of the visit exists, the result closer to the planned visit in the protocol is considered as the result of the visit and is included in the analysis. If the absolute value of the difference between visits is the same based on the planned visit (e.g. -3 days, +3 days) previously measured results (day -3) are considered the results of the visit and included in the analysis. We also analyze the results of unscheduled visit in the same way. Listing presents the results of all visits, including unscheduled visits, regardless of whether or not the analysis visit is included.

The analysis visit is calculated as the measurement date, not the visit date.

Table 2 Analysis visit definition – 0-8 Vaccination schema

Analysis visit	Visit day Interval (days)	Visit window (days)	Analysis visit permitted window (days)
Visit 1 (Baseline)	0		
Visit 2	7	$\pm$ 2	5 $\leq$ Visit 2-Baseline$\leq$ 9
Visit 3	56	$\pm$ 3	53 $\leq$ Visit 3-Baseline$\leq$ 59
Visit 4	84	$\pm$ 3	81 $\leq$ Visit 4-Baseline$\leq$ 87
Visit 5	112	$\pm$ 4	108 $\leq$ Visit 5-Baseline$\leq$ 116
Visit 6	168	$\pm$ 7	161 $\leq$ Visit 6-Baseline$\leq$ 175
Visit 7	252	$\pm$ 7	245 $\leq$ Visit 7-Baseline$\leq$ 259
Visit 8	336	$\pm$ 7	329 $\leq$ Visit 8-Baseline$\leq$ 343

Table 3 Analysis visit definition – 0-12 Vaccination schema

Analysis visit	Visit day Interval (days)	Visit window (days)	Analysis visit permitted window (days)
Visit 1(Baseline)	0		
Visit 2	7	$\pm$ 2	5 $\leq$ Visit 2-Baseline$\leq$ 9
Visit 3	84	$\pm$ 3	81 $\leq$ Visit 3-Baseline$\leq$ 87
Visit 4	112	$\pm$ 3	109 $\leq$ Visit 4-Baseline$\leq$ 115
Visit 5	140	$\pm$ 4	136 $\leq$ Visit 5-Baseline$\leq$ 144
Visit 6	168	$\pm$ 7	161 $\leq$ Visit 6-Baseline$\leq$ 175
Visit 7	252	$\pm$ 7	245 $\leq$ Visit 7-Baseline$\leq$ 259
Visit 8	336	$\pm$ 7	329 $\leq$ Visit 8-Baseline$\leq$ 343

8.4 Derived or transformed variables

The baseline is defined as last non-missing value on or prior to the start date of IP administration.

Table 4 Derived Variables

Variables	Method
Change from baseline	Post-baseline value – Baseline value
Age group	Age < 66y old, Age $\geq$ 66y old
Total dose (mg)	Sum of investigational product doses at each time point
GMT	10^(Mean of $\log_{10} value$)

Variables	Method
Change from baseline (GMT)	10^(Mean of $(\log_{10}\text{post} - \text{baseline value} - \log_{10}\text{baseline value})$)
GMR	$10^{(\log_{10} GMT1 - \log_{10} GMT2)}$
AE Duration (days)	AE end date – AE start date+1 if AE end date is ongoing, replaced with last visit date and add symbol (≥) (ex. ≥15)
Occurrence Duration (days)	AE start date – Investigational product start date

9. Subject Information

Subject information will be analyzed on ITT.

9.1 Subject Disposition

The following subjects or reason will be summarized using number of subjects and percentages by vaccination group and overall. The screened, screened fail and study completion status of subjects will also be summarized by study sites using number of subjects and percentages by vaccination group and overall.

- Screening/Screening fail
- Reason for Screening fail
- Follow-up continued (V4)/Discontinued (V4)
- Study Completed/Discontinued
- Reason for discontinuation

9.2 Protocol Deviation

Subjects who are excluded from analysis sets (ITT, mITT, SS, and PPS) and the details will be presented in a listing.

9.3 Analysis Sets

The number of subjects included in each population set (ITT, mITT, SS, and PPS) and the percentages will be summarized by vaccination group. The reasons of exclusion from each set will also be summarized using number of subjects and percentages by vaccination group.

9.4 Demographics and Baseline Characteristics Analyses

Demographics and Baseline Characteristics will be summarized on mITT.

9.4.1 Demographics and Baseline Characteristics

For the following variables, the continuous variables will be summarized with number of subjects, mean, standard deviation, median, minimum, and maximum by vaccination group. The categorical variables will be summarized using number of subjects and percentages by vaccination group.

- Age(years), Age group (<66y old, ≥66y old, for Phase IIa), Sex, Fertility status, Alcohol, Smoking
- Alcohol consumption (Units/week), Height (cm), Weight (kg), BMI (kg/m^2)
- 12-Lead Electrocardiogram (ECG) : Heart rate (bpm), PR (msec), QRS (msec), QT (msec), QTcF (msec), ECG result, PCR/Antibody test results for SARS-CoV-2 infection at baseline)

9.4.2 Medical History and Comorbidities

Previous medical history will be defined as those that are checked "No" for the question "Ongoing" under [Medical History] page of the CRF, and comorbidities will be defined as those that are checked "Yes" for the same question.

Medical history and comorbidities will be coded with medical dictionary for regulatory activities (MedDRA) version 25.0 and will be summarized with system organ class (SOC) and preferred term (PT) by vaccination group using number of subjects and percentages.

9.4.3 Prior and Concomitant Medications

Prior medication will be defined as any medication that the subjects took in past 24 weeks and stopped prior to the first vaccination of investigational product. Only, prior medications associated with exclusion criteria will be recorded based on the time point of taking the medications.

Concomitant medication will be defined as any medication that the subjects took after the first vaccination of investigational product, including any prior medications that were ongoing at the time of first vaccination.

Prior medication classification

- Medication start date < Date of first vaccination of investigational product (Date of V1) or
- Medication end date ≤ Date of first vaccination of investigational product (Date of V1)

Concomitant Medications classification

- Medication start date ≥ Date of first vaccination of investigational product (Date of V1) or
- Medication end date ≥ Date of first vaccination of investigational product (Date of V1) or
- Ongoing

Prior and concomitant medications will be coded using world health organization anatomical therapeutic

chemical index (WHO ATC index) 2022 and will be summarized with level1 (anatomical main group) and level 5 (chemical substance) by vaccination group using number of subjects and percentages. If level 5 (chemical substance) does not exist or 'Combinations' and/or 'Various', higher level will be used instead.

10. Safety and Tolerability Analyses

Safety and tolerability analyses will be performed on SS.

10.1 Extent of Exposure

Total number of vaccinations (times) and total dose (mg) will be summarized with number of subjects, mean, standard deviation, median, minimum, and maximum by vaccination group.

* Total dose is defined as sum of study drug doses at each time point.

- Total Dose in Placebo / GLS-5310 0.6 mg / GLS-5310 1.2 mg (8W) / GLS-5310 1.2 mg (Re-vac.) = Dose at Baseline + Dose at Week 8
- Total dose in GLS-5310 1.2 mg (12W) = Dose at Baseline + Dose at Week 12

10.2 Adverse Events

An adverse event (AE) is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body, or worsening of a pre-existing condition, temporally associated with the use of a product whether or not considered related to the use of the product.

Frequencies will be presented with respect to maximum severity and to strongest relationship to vaccination of the investigational product. Multiple occurrences of the same AE will be counted only once following a worst-case approach with respect to severity and relationship to vaccination of the investigational product.

Treatment-emergency adverse event (TEAE) refers to any AE that did not exist prior to vaccination of the investigational product, but that occurred after the initial vaccination of the investigational product, or a pre-existing condition that worsens after the initial vaccination of the investigational product.

Adverse drug reaction (ADR) is any noxious and unintended response to a medicinal product related to any dose, which a causal relationship between a medicinal product and an adverse event cannot be ruled out. An ADR includes reactions that represent an unexpected worsening of an existing medical condition. The following relationship categories will be considered as ADR:

- Probably related
- Possibly related

A serious adverse event (SAE) is any AE that meets one of the following conditions:

- Death
- Life-threatening events
- An event requiring inpatient hospitalization or prolongation of existing hospitalization during the period of protocol defined surveillance (including any overnight stay in the hospital, regardless of the length of stay, even if the hospitalization is only a precautionary measure to allow continued observation. NOTE: Evaluation in a physician's office, or at a hospital or other urgent care setting in an observational, non-admitted status regardless of the time period of observation, does not constitute an SAE
- Events resulting in congenital anomaly or birth defect
- Events that cause persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions
- Other important medical events that may not result in death, are life threatening, or require hospitalization, but are considered as serious by the Investigator. Examples of such medical events include anaphylaxis, new onset seizures

An Adverse Events of Special Interest is an enhanced disorder of the immune system relationship, and the following symptoms can be observed more closely.

- Documented vital sign showing respiratory rates is 30 breaths or greater per minutes, heart rate is 125 beats or greater per minute, SpO2 is 93% or less in indoor air, or PaO2 / FiO2 is less than 300 mmHg.
- Respiratory failure (In case of requirement for high flow oxygen, non-invasive ventilation, mechanical ventilation or ECMO)
- Shock (systolic blood pressure < 90 mmHg or diastolic blood pressure < 60 mmHg or requiring vascular inhibitor)
- Severe acute renal failure, liver or neurological dysfunction
- Intensive Care Unit (ICU) admission
- Death

TEAEs leading to vaccination discontinuation is defined as TEAE that Action taken with IP is stopping vaccination.

10.2.1 Summary of Adverse Events

The following types of all AEs will be summarized with the number of subjects, incidence (%), 95% Clopper-Pearson's confidence interval and the number of events. In Phase IIa analysis, the differences in proportion between the groups will also be calculated with exact 95% confidence interval (Chan and Zhang 1999).

The Solicited local AEs and Solicited Systemic AEs will be summarized for all TEAEs, all ADRs, all SAEs and all SADRs.

- TEAEs
- ADRs
- SAEs
- SADRs
- TEAEs leading to vaccination discontinuation
- Adverse Events of Special Interest

10.2.2 Analysis Adverse Events

The following types of AEs will be coded with medical dictionary for regulatory activities (MedDRA) version 25.0 and will be summarized with system organ class (SOC) and preferred term (PT) by vaccination group using number of subjects, percentages, and number of events.

- TEAEs
- ADRs
- All Serious TEAEs
- Serious adverse drug reaction (SADR)
- All TEAEs leading to vaccination discontinuation
- Adverse Events of Special Interest
- TEAEs by severity (toxicity grade)
- ADRs by severity (toxicity grade)
- TEAEs by relationship to the investigational product
- Solicited local TEAEs
- Solicited local ADRs
- Solicited local SAEs
- Solicited local SADR
- Solicited systemic TEAEs
- Solicited systemic ADRs
- Solicited systemic SAEs
- Solicited systemic SADR

The details of SAEs will also be presented in a listing.

The details of Solicited local/systemic SAEs will also be presented in a listing.

10.3 VAS Scores

VAS score will be summarized by each timepoint using number of subjects, mean, standard deviation, median, minimum, and maximum by vaccination group.

10.4 Laboratory Evaluations

For numeric laboratory parameters that contain inequality signs in the results, only the numeric portion of the results will be used in the analysis removing the inequality signs (e.g., '<1.002' will be analyzed as '1.002').

Continuous parameters will be summarized by each timepoint and the changes from baseline to each timepoint using number of subjects, mean, standard deviation, median, minimum, and maximum by vaccination group.

Categorical parameters will be classified into Normal/NCS (not clinically significant) or CS (clinically significant) and the changes from baseline to each timepoint will be presented as a shift table by vaccination group.

Compare the laboratory results with the normal range will be classified into Low (<Lower limit), Normal(include normal range), High (>Upper limit) and the changes from baseline to each timepoint will be presented as a shift table by vaccination group.

The analysis units of laboratory parameters are as follows.

Table 5 Units of Laboratory Parameters

Hematology		Biochemistry	
Parameter	**Unit**	**Parameter**	**Unit**
RBC	$10^6/\mu L$	Glucose	mg/dL
Hemoglobin	g/dL	BUN	mg/dL
Hematocrit	%	Creatinine	mg/dL
Platelet	$10^3/\mu L$	Uric acid	mg/dL
WBC	$10^3/\mu L$	Total protein	g/dL
Neutrophil	%	Albumin	g/dL
Lymphocyte	%	Total bilirubin	mg/dL
Monocyte	%	ALP	IU/L
Eosinophils	%	AST	IU/L
Basophils	%	ALT	IU/L
		GGT	IU/L
		Total Cholesterol	mg/dL

Hematology		Biochemistry	
Parameter	**Unit**	**Parameter**	**Unit**
		CPK	IU/L
		Na	mmol/L
		K	mmol/L
		P	mg/dL
		Cl	mmol/L
		Ca	mg/dL
		Mg	mEq/L

The details of parameters that are clinically significant after baseline will be presented in a listing with results for all timepoints.

10.5 Vital Signs

The following parameters will be summarized by each timepoint and change from baseline with number of subjects, mean, standard deviation, median, minimum, and maximum by vaccination group.

- Vital Sign parameters: Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg), Heart rate (beats/min), Respiratory rate (breaths/min), Body temperature (°C)

11. Immunogenicity Analysis

Immunogenicity analysis will be performed on mITT, PP with sufficient sample to assay.

The immounogenicity parameters are as follows.

Table 6 In the immunogenicity evalatuion category, positivity is classified according to the following criteria.

Immunogenicity			
Endpoints	**Parameter**	**Unit**	**Criteria for Positive/Negative (or Responder/Non-Responder)**
Binding antibody	S-ELISA	Endpoint Titer	Threshold limit to be considered as having a positive response is >50
	ORF3a-ELISA	Endpoint Titer	Threshold limit to be considered as having a positive response is >50
Neutralizing antibody	NEUT	NT_{50}	Cutoff value on a per-subject basis is defined as: 4x that subject's Day 0 response.
T cell response	ELISPOT	SFU per 10^6 cells	Cutoff value on a per-subject basis is defined as: 2x that subject's Day 0 response. If there is no Day 0 data for that subject, then the cutoff is defined as 2x average Day 0 response for all study participants

11.1 Binding Antibody Responses

The binding antibody response will be classified as responder/non-responder and will be analyzed as the frequency of responses for each assay for each treatment arm at each time point at which an assessment is performed. Estimates of proportions and exact 95% Clopper-Pearson's confidence interval and exact 95% confidence interval (Chan and Zhang 1999) for the differences between the groups will be calculated. Comparison between treatment arms will be carried out using a Fisher's exact test. However, Part 1 of the study is not powered to distinguish statistical differences between dosing regimens.

The group geometric mean titer (GMT) for binding antibody endpoint titers for the SARS-CoV-2 will be calculated and the 95% confidence interval will be presented. The comparison among the administration groups of GMT will be analyzed using a two-sample t-test. Also, the geometric mean titer ratio will be calculated and its 95% confidence interval will be provided. For the GMT and the mean fold increase in GMT from baseline, the mean of the antibody that was transformed by log10 and the 95% confidence interval will be calculated and then changed back to the original unit.

11.2 Neutralizing Antibody Responses

The neutralizing antibody response will be classified as responder/non-responder and will be analyzed as the frequency of responses for each assay for each treatment arm at each time point at which an assessment is performed. Estimates of proportions and exact 95% Clopper-Pearson's confidence interval and exact 95% confidence interval (Chan and Zhang 1999) for the differences between the groups will be calculated. Comparison between treatment arms will be carried out using a Fisher's exact test. However, Part 1 of the study is not powered to distinguish statistical differences between dosing regimens.

The group geometric mean titer (GMT) for neutralizing antibody for the SARS-CoV-2 will be calculated and the 95% confidence interval will be presented. The comparison among the administration groups of GMT will be analyzed using a two-sample t-test. Also, the geometric mean titer ratio will be calculated and its 95% confidence interval will be provided. For the GMT and the mean fold increase in GMT from baseline, the mean of the antibody that was transformed by log10 and the 95% confidence interval will be calculated and then changed back to the original unit.

11.3 T cell Responses

The T cell response will be classified as responder/non-responder and will be analyzed as the frequency of

responses for each assay for each treatment arm at each time point at which an assessment is performed. Estimates of proportions and exact 95% Clopper-Pearson's confidence interval and exact 95% confidence interval (Chan and Zhang 1999) for the differences between the groups will be calculated. Comparison between treatment arms will be carried out using a Fisher's Exact Test. However, Part 1 of the study is not powered to distinguish statistical differences between dosing regimens.

12. Changes to Protocol-Specified Analysis

The following exploratory endpoints were already performed before. Therefore, this version of the SAP does not include analysis as below.

Phase I Exploratory Objectives

- Determine IgG antibody responses after a single dose of vaccine related to treatment arm

Phase IIa Exploratory Objectives

- Determine the persistence of immune responses following vaccination with GLS-5310
- Determine the extent of immune boosting responses for participants who are seropositive at baseline following vaccination with GLS-5310

In addition, in the Phase I exploratory evaluation, analysis method to 'Assess the effectiveness of preventing lung infection when the SARS-CoV-2 virus is attacked after manually transferring the vaccinated serum to viral challenged animal model' was not included in this SAP because the analysis has already been completed and the non-clinical results report has been created. Other exploratory evaluations have been contained in immunogenicity analysis.

13. Reference

None.

14. Role and Responsibility

Roles and responsibilities of this study are as following.

Table 7 Role and Responsibility

Role	Name	Responsibility
Biostatistician	Kim, hyunah	Statistical analysis
Senior Biostatistician	Ma, bogyoung	Quality control for the statistical analysis process

Role	Name	Responsibility
Biostatistics Manager	Ma, bogyoung	Approval for SAP

15. Applied SOPs

The following SOPs of C&R Research will be applied in this study.

Table 8 Applied SOPs

SOP No.	SOP Version	SOP Name
0400	3.0	Statistical Analysis Plan
0401	5.3	Statistical Analysis Process
0404	3.0	Random Code Break Process
0406	4.0	Definition of Analysis Population
0407	3.0	Blind Data Review Report Writing
0408	3.0	Statistical Analysis Document Management
0450	1.0	Statistical Programming Process

16. Applied SOP SDs

The following SDs of C&R Research will be used in this study.

Table 9 Applied SOP SDs

SD No.	SD Version	SD Title
SD 0400 A	3.0	Statistical Analysis Plan
SD 0401 A	4.1	Statistical Analysis QC Report
SD 0401 B	4.1	Analysis Dataset Specification
SD 0404 A	2.0	Unblinding Request Form
SD 0404 B	2.0	Unblinding Authorization Form for Statistical Analysis
SD 0406 A	5.0	Definition of Analysis Population
SD 0407 A	3.0	Blind Data Review Report
SD 0408 A	4.0	STAT Master File Index

17. Changes to Laboratory Parameters Units

None.

18. TLF shell

Tables and lists of studies are attached in the appendix “[별첨] CoV2-001_TLFs_v1_0.xlsx”.

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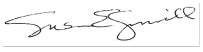
Signature	

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Protocol	CoV2-001
Document Title	Statistical Analysis Plan