Protocol: J2Z-MC-PGAA (c)

A Phase 1, Randomized, Placebo-Controlled Study to Evaluate the Tolerability, Safety, Pharmacokinetics, and Immunogenicity of LY3832479 Given as a Single Intravenous Dose in Healthy Participants

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Approval Date: 15-Jul-2020

Title Page

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Protocol Number: J2Z-MC-PGAA

Amendment Number: c

Compound: LY3832479

Study Phase: 1

Short Title: A Phase 1, Randomized, Placebo-Controlled Study to Evaluate LY3832479 in Healthy Participants

Sponsor Name: Eli Lilly and Company
Legal Registered Address: Indianapolis, Indiana USA 46285

Regulatory Agency Identifier Number(s)

Pre-IND number: 150707

Approval Date: Protocol Electronically Signed and Approved by Lilly on the date provided below.

Approval Date: 15-Jul-2020 GMT

Medical Monitor Name and Contact Information will be provided separately.

Protocol Amendment Summary of Changes Table

DOCUMENT HISTORY	
Document	**Date**
Original Protocol	03-Jun-2020
Amendment (a)	23-Jun-2020
Amendment (b)	26-Jun-2020

Amendment (c)

Overall Rationale for the Amendment:

Language has been added throughout the protocol to allow for collection of additional swab samples, some of which may be used for research purposes.

Section # and Name	Description of Change	Brief Rationale
Section 1.3 (Schedule of Activities); Section 5.1 (Inclusion Criteria)	Added reference to post-baseline nasal or nasopharyngeal swab.	To facilitate analysis of postbaseline samples for research purposes.
Section 8.3.7, (SARS-Cov-2 Infection); Section 8.8 (Biomarkers)	Added description of how and when post-baseline nasal or nasopharyngeal swab will be administered.	As above.
Section 10.2 (Appendix 2: Clinical Laboratory Tests)	Added detail of how post-baseline nasal or nasopharyngeal sample will be managed.	As above.

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1. Protocol Summary

1.1. Synopsis

Protocol Title: A Phase 1, Randomized, Placebo-Controlled Study to Evaluate the Tolerability, Safety, Pharmacokinetics, and Immunogenicity of LY3832479 Given as a Single Intravenous Dose in Healthy Participants

Short Title: A Phase 1, Randomized, Placebo-Controlled Study to Evaluate LY3832479 in Healthy Participants

Rationale:

Lilly is developing LY3832479 for the treatment and prevention of coronavirus disease 2019 (COVID-19). Study J2Z-MC-PGAA (PGAA) will investigate the safety, tolerability, and pharmacokinetics of LY3832479 when administered as a single intravenous dose to healthy participants.

Objectives and Endpoints

Objectives	Endpoints
Primary	
• To investigate the safety and tolerability of a single dose of LY3832479 in healthy participants	• Serious and nonserious adverse events, laboratory measures of safety, ECG, and vital signs
Secondary	
• To characterize the pharmacokinetics of LY3832479 following a single IV administration of LY3832479 to healthy participants	• AUC, Cmax

Abbreviations: AUC = area under the concentration versus time curve; Cmax = maximum observed drug concentration; ECG = electrocardiogram; IV = intravenous.

Overall Design

Study PGAA is a Phase 1, randomized, placebo-controlled study of LY3832479 administered to healthy participants.

The study will comprise up to 3 cohorts, each with an intended number of participants as follows:

<u>Cohorts 1 and 2</u>

At least 9 participants:

- 7 randomized to LY3832479 and
- 2 randomized to placebo.

Cohort 3

At least 8 participants:

- 6 randomized to LY3832479 and
- 2 randomized to placebo.

Participants will be initially monitored for safety within the study site where they will be admitted on Day -1, dosed on Day 1, discharged on Day 4, and subsequently monitored on an outpatient basis until the last follow-up visit.

Disclosure Statement: This is a sequential, single-ascending dose study with up to 3 cohorts that is participant and investigator blinded.

Number of Participants:

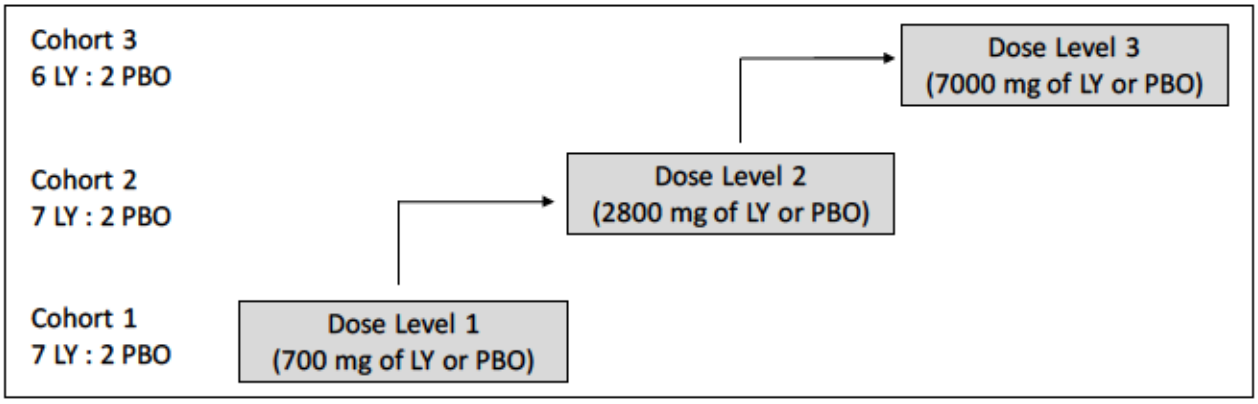
A maximum of 30 participants will be enrolled to study intervention such that approximately 8 participants have sufficient evaluable data in each of the 3 cohorts.

Intervention Groups and Duration:

Single-dose study with an estimated duration for each participant of up to 16 weeks from screening through follow-up.

Data Monitoring Committee: No

1.2. Schema



Abbreviations: LY = LY3832479; PBO = placebo; PK = pharmacokinetics.

Note: After at least 7 participants have completed Day 4 in a given cohort, all safety data up to this cutoff date will be reviewed to determine whether the next cohort can be enrolled after agreement between Lilly's medical monitor and the investigator.

Figure 1. Single-ascending dose schema for Study J2Z-MC-PGAA.

1.3. Schedule of Activities (SoA)

Procedure / Assessments	Screening	Dosing					Postdose Follow-up Visits								Comment
Visit Number	V1	V2					V3	V4	V5	V6	V7	V8	V9	V10/ ED	
Week(s)		0					1	2	3	4	6	8	10	12	
Study Day	-14 to –2	-1	1	2	3	4	8 ±1d	15 ±2d	22 ±2d	29 ±3d	43 ±3d	57 ±3d	71 ±3d	85 ±3d	
Informed consent (written)	X														
Review/confirm inclusion/exclusion criteria	X	X	Predose												After screening, ensure participants continue to meet I/E criteria.
Medical history including pre-existing conditions	X														
Weight/height	X													X	Height at screening only.
Urinalysis	X														
COVID-19 clinical screening	X	X					X	X	X	X	X	X	X	X	Symptoms and recent contact (see Section 8.3.7 for a description of symptoms and close contact). At screening, Day -1 and as needed during the study. See Section 4.1 for details.
SARS-CoV-2 serology		X						X		X		X		X	Serology results are not needed before dosing.

Procedure / Assessments	Screening	Dosing					Postdose Follow-up Visits								Comment
Visit Number	V1	V2					V3	V4	V5	V6	V7	V8	V9	V10/ ED	
Week(s)		0					1	2	3	4	6	8	10	12	
Study Day	-14 to –2	-1	1	2	3	4	8 ±1d	15 ±2d	22 ±2d	29 ±3d	43 ±3d	57 ±3d	71 ±3d	85 ±3d	
Nasal or nasopharyngeal swab	X														At screening, only if SARS-CoV-2 point-of-care test will not be available for Day -1. Post-baseline, additional nasal or nasopharyngeal swabs may be conducted for research purposes. See Section 8.3.7.
Admission to study site/check in (admission day may vary depending on IP availability)		X													If screening is conducted within 3 days of check-in, participants may stay at the study site between screening and check in. See Section 4.1 for details.
SARS-CoV-2 point-of-care test		X													On Day -1, if nasal/nasopharyngeal swab was not performed at screening. Additional point-of-care tests may be conducted at the investigator's discretion. See Section 8.3.7.
Discharge from study site						X									

Procedure / Assessments	**Screening**	**Dosing**					**Postdose Follow-up Visits**								**Comment**
Visit Number	**V1**	**V2**					**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**V10/ ED**	
Week(s)		**0**					**1**	**2**	**3**	**4**	**6**	**8**	**10**	**12**	
Study Day	**-14 to –2**	**-1**	**1**	**2**	**3**	**4**	**8** ±1d	**15** ±2d	**22** ±2d	**29** ±3d	**43** ±3d	**57** ±3d	**71** ±3d	**85** ±3d	
Physical examination (PE)/Medical assessment (MA)	X	X	Predose			X	As needed							X	Full PE/MA at screening and Visit 10/ED. Symptom-directed PE/MA at all other indicated time points and as deemed necessary by the investigator.
Vital signs: blood pressure, pulse rate[a]	X	X	Predose, every 15 min during infusion; every 30 min until 2h after **end** of infusion; then every 60 min until 6h after **end** of infusion.	24 h (±2 h)	48 h (±2 h)	X	X	X	X	X	X	X	X	X	Vital signs should be taken following an at least 5-min rest in a supine position. Vital signs may be taken any time prior to dosing.
Body temperature	X	X	Predose, 6 h (±15 min)	24 h (±2 h)											May be performed at additional time points at the discretion of the investigator.
Single 12-lead ECG[a]	X		Predose, 1 h (±10 min), 6 h (±15 min)	24 h (±2 h)	48 h (±2 h)		X	X		X				X	All ECGs are local. Predose ECG can be taken any time prior to dosing on same day.

Procedure / Assessments	**Screening**	**Dosing**					**Postdose Follow-up Visits**								**Comment**
Visit Number	**V1**	**V2**					**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**V10/ ED**	
Week(s)		**0**					**1**	**2**	**3**	**4**	**6**	**8**	**10**	**12**	
Study Day	**-14 to –2**	**-1**	**1**	**2**	**3**	**4**	**8** ±1d	**15** ±2d	**22** ±2d	**29** ±3d	**43** ±3d	**57** ±3d	**71** ±3d	**85** ±3d	
Concomitant medications and AE review	X	X	Predose	X	X	X	X	X	X	X	X	X	X	X	AE only after participant has signed the study informed consent form.
HIV, hepatitis B/C serology	X														
Pregnancy test (women only)[b]	X	X													Serum pregnancy test at screening. Day -1 urine test refers to test at check-in; this is not needed if check-in occurs on same day as screening. Postdose urine test(s) can be performed at the judgment of the investigator, if pregnancy is suspected.
Clinical laboratory tests[a]	X		Predose		X		X	X	X	X	X	X		X	Fasting is not required for these tests.

Procedure / Assessments	Screening	Dosing					Postdose Follow-up Visits								Comment
Visit Number	V1	V2					V3	V4	V5	V6	V7	V8	V9	V10/ ED	
Week(s)		0					1	2	3	4	6	8	10	12	
Study Day	-14 to –2	-1	1	2	3	4	8 ±1d	15 ±2d	22 ±2d	29 ±3d	43 ±3d	57 ±3d	71 ±3d	85 ±3d	
Breath or urine ethanol screen		X													Ethanol test is on the day of check-in. If screening visit is the same as day of check-in, no further ethanol test is required. Ethanol screen may be repeated at other time points at the discretion of the investigator.
Urine drug screen	X	X													Day -1 urine test refers to test at check-in; this is not needed if check-in occurs on same day as screening. Drug screen may be repeated at other time points at the discretion of the investigator.
IV LY3832479 or placebo dosing			X												Participants will be randomized to receive either LY3832479 or placebo. Dosing may be delayed due to IP being unavailable; see Section 4.1.

Procedure / Assessments	Screening	Dosing					Postdose Follow-up Visits								Comment
Visit Number	V1	V2					V3	V4	V5	V6	V7	V8	V9	V10/ ED	
Week(s)		0					1	2	3	4	6	8	10	12	
Study Day	-14 to –2	-1	1	2	3	4	8 ±1d	15 ±2d	22 ±2d	29 ±3d	43 ±3d	57 ±3d	71 ±3d	85 ±3d	
LY3832479 PK sampling[a]			Predose, end of infusion (±10 mins), 6 hours (±30 mins) after start of infusion.	24 h (±2 h)	48 (±2 h)		X	X		X	X	X		X	Predose collection should be taken within 15 min before dosing. The exact time of draw must be recorded.
Immunogenicity sample[a]			Predose					X		X		X		X	
Serum sample for exploratory biomarkers[a]			X		X			X		X		X		X	
Pharmacogenetics sample[a]			Predose												For storage only.

Abbreviations: AE = adverse event; COVID-19 = coronavirus disease 2019; ECG = electrocardiogram; ED = early discontinuation; HIV = human immunodeficiency virus; I/E = inclusion/exclusion criteria; IV = intravenous; PK = pharmacokinetics; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; V = Visit

a When conducted on the same day, the order of procedures should be vital signs, ECG, and then blood sampling.

b For women who are considered to be postmenopausal, follicle-stimulating hormone should be drawn to confirm postmenopausal status if necessary, according to Appendix 4 (Section 10.4).

2. Introduction

Given the current epidemiologic emergency caused by the coronavirus disease 2019 (COVID-19) pandemic, Eli Lilly and Company (Lilly) is seeking opportunities to identify potential prophylactic and treatment options to help in the prevention and control of this public health issue. Recently, Lilly entered into a co-development agreement with TopAlliance Biosciences, Inc. to develop LY3832479 (also known as JS016-CB6, JS016, or CB6). LY3832479 is a recombinant, fully human neutralizing monoclonal immunoglobulin (Ig) G1 kappa antibody with abrogated Fc effector function.

2.1. Study Rationale

Lilly is developing LY3832479 for the treatment and prevention of COVID-19. Study J2Z-MC-PGAA (PGAA) will investigate the safety, tolerability, and pharmacokinetics (PK) of LY3832479 when administered as a single intravenous (IV) dose to healthy participants.

2.2. Background

The viral pathogen causing the COVID-19 pandemic is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Viral entry into host cells involves its structural Spike glycoprotein. The Spike glycoprotein attaches itself via its receptor-binding domain (RBD) to the human angiotensin-converting enzyme 2 (ACE2), enabling sufficient proximity for the virus to fuse with the target cell membrane. ACE2 is expressed in the membrane of various cell types in a variety of tissues, primarily in the lung, small intestine, kidney, and vascular endothelium (Hamming et al. 2004; Human Protein Atlas Project website [WWW]).

LY3832479 specifically binds the Spike glycoprotein RBD with high affinity, preventing its interaction with the ACE2 human receptor. This in turn blocks viral cell fusion, preventing SARS-CoV-2 invasion of human cells, inhibiting viral replication. As the binding epitope of LY3832479 to RBD covers the most conserved RBD/ACE2 interaction site based on an analysis of the LY3832479-RBD complex x-ray structure, LY3832479 is expected to neutralize all currently described viral strains.

The amino acid sequence of recombinant antibody LY3832479 was derived from human memory B cells of a convalescent patient with COVID-19. Therefore, formation of antidrug antibodies (ADAs) and related side effects is unlikely. To further reduce potential toxicity to human cells, point mutations (L234A, L235A; LALA mutation) were introduced into the Fc domain of the native human IgG1 antibody to eliminate Fc effector function, to reduce the risk of antibody-dependent enhancement (ADE).

2.3. Benefit/Risk Assessment

Concurrent with Study PGAA, LY3832479 is being developed in China in an ongoing Phase 1 clinical study in healthy participants, Study JS016-001-I. The first cohort of Study JS016-001-I was dosed on 07 June 2020, with 3 participants receiving a single infusion of 2.5 mg/kg of LY3832479 and 1 participant receiving placebo. As of 23 June 2020, LY3832479 was well

tolerated. The only adverse event reported was a mild and transient increase in serum creatinine in 1 participant.

The nonclinical safety package includes the following studies listed.

- a single-dose toxicology/toxicokinetic (TK) study that also evaluates the TK of LY3832479 in cynomolgus monkeys.
- A good laboratory practice (GLP)-compliant 21-day repeat-dose (25, 75, 205 mg/kg every 3 days) study in cynomolgus monkeys with a 6-week recovery period. This study evaluated TK and safety pharmacology.
- GLP-compliant tissue cross-reactivity (TCR) studies in human and cynomolgus tissues.

An interim report including in-life data from the dosing phase for the repeat-dose study was available at the time of the initial IB. An additional interim report including histopathology, respiratory function and TK data is expected to be available early during the conduct of this Phase 1 study. A final report for the repeat-dose study is expected to be submitted after the completion of the recovery phase. The IB will be updated when additional information is reported.

The preclinical studies being carried out support the clinical development of LY3832479 against a foreign target.

Although there is an ongoing first-in-human clinical study testing LY3832479 in healthy participants in China (Study JS016-001-I), only limited data from that study are available at this time. Therefore, Study PGAA has been designed to be conducted in accordance with principles outlined in the Guideline on Strategies to Identify and Mitigate Risks for First-in-Human Clinical Trials with Investigational Medicinal Products (EMA 2017). Any identified risks are considered to be monitorable and manageable at the planned dose range of 700 to 7000 mg LY3832479 in healthy participants.

There is no anticipated therapeutic benefit for the participants.

Theoretical risks related to infusion of LY3832479 are:

- Severe acute infusion reaction. This risk is decreased due to
    - LY3832479 being directed against a foreign target
    - the human origin of LY3832479, and
    - the reduced Fc effector function
- Other hypersensitivity reactions as for any other protein product
- Antibody-dependent enhancement of viral replication in case any of these healthy volunteers contract a SARS-CoV-2 infection while they still have significant LY3832479 exposure after a single IV infusion. This phenomenon has been observed with some other viruses including the dengue virus, but is only a theoretical risk without clinical evidence in the case of respiratory coronaviruses (Graham 2020). In addition, LY3832479 was specifically engineered to avoid this risk as explained in Section 2.2.
- Unknown risks related to on-target and off-target toxicity. These risks are low due to the
    - fact that LY3832479 targets a foreign protein,
    - human origin of LY3832479 (the LALA mutations do not involve the RBD of LY3832479), and

- absence of binding in the TCR studies performed in humans and monkeys.

More detailed information about the known and expected benefits and risks and reasonably expected adverse events (AEs) of LY3832479 may be found in the IB.

3. Objectives and Endpoints

Objectives	Endpoints
Primary	
• To investigate the safety and tolerability of a single dose of LY3832479 in healthy participants	• Serious and nonserious adverse events, laboratory measures of safety, ECG, and vital signs
Secondary	
• To characterize the pharmacokinetics of LY3832479 following a single IV administration of LY3832479 to healthy participants	• AUC, Cmax

Abbreviations: AUC = area under the concentration versus time curve; Cmax = maximum observed drug concentration; ECG = electrocardiogram; IV = intravenous.

4. Study Design

4.1. Overall Design

Study PGAA is a Phase 1, randomized, placebo-controlled study of LY3832479 administered to healthy participants.

Screening

Each participant will provide informed consent for study participation and will undergo a screening examination within 14 days prior to enrollment.

Participants may be offered the possibility of staying at the study site between screening and dosing. In addition, the day of dosing may be delayed by up to 3 days in the event investigational product is unavailable.

The day of dosing will always be designated as Day 1, the day before dosing will always be designated as Day -1, and subsequent activities carried out per the timings in the SoA.

Participants will be discharged on Day 4, and subsequently monitored on an outpatient basis until the last follow-up visit.

In the event of such a delay, the following assessments conducted on Day -1 should be repeated on subsequent days until dosing:

- COVID-19 clinical screening,
- review/confirm eligibility criteria,
- vital signs,
- body temperature,
- concomitant medications, and
- adverse events.

4.1.1. Single-Ascending Dose Design

The study will comprise up to 3 cohorts, each with an intended number of participants as follows:

Cohorts 1 and 2
At least 9 participants

- 7 randomized to LY3832479 and
- 2 randomized to placebo.

Cohort 3
At least 8 participants

- 6 randomized to LY3832479 and
- 2 randomized to placebo.

A maximum of 30 participants will be enrolled to study intervention such that approximately 8 participants have sufficient evaluable data in each cohort.

After at least 7 participants have completed Day 4 in a given cohort (see Section 4.2 for rationale), all safety data up to this cutoff date will be reviewed to determine whether the next cohort can be dosed, as well as the dose to be used, after agreement between the Lilly's medical monitor and the investigator. Safety and tolerability data will be the primary criteria guiding dose escalation.

The investigator and the Lilly sponsor team are responsible for determining any dose decisions. The investigator(s) will remain blinded and the Lilly sponsor team will be unblinded during these reviews. All available data from previous cohorts will be reviewed.

4.2. Scientific Rationale for Study Design

This study is designed to explore a range of doses that will inform the clinical drug development plan for LY3832479.

The sequential cohort, single-dose escalation design with safety reviews before each cohort will minimize safety risks to participants during dose exploration.

Sentinel dosing is not included in this design as LY3832479 is not considered a high uncertainty compound based on its origin, structure, mechanism of action/pharmacology target (it is directed against a foreign target), and nonclinical data:

- No toxicity was observed in the single-dose monkey TK study (study report pending).
- LY3832479 is a monoclonal antibody (mAb) directed against a foreign target and was isolated from a convalescent patient with COVID-19; therefore, it has a low risk for on-target or off-target toxicity.
- The risk of infusion-related reaction is considered low due to the target, the reduced effector function (Fc and Complement binding), and the human origin of this antibody.
- The engineered LALA mutations are expected to reduce Fc effector function in LY3832479 and should reduce the risk of ADE.

The 4-day safety review after dosing is sufficient to detect an acute adverse immune response to treatment with LY3832479 that would preclude dose escalation.

4.3. Justification for Dose

The dose levels for this study are designed to explore a wide exposure range that potentially encompasses the therapeutic dose, and will provide the safety and tolerability underpinnings for the clinical drug development plan for LY3832479. Due to the uncertainty of in vitro to in vivo translation and uncertainty in translation of data from a rhesus macaque SARS-CoV-2 infection model to humans, 3 methods were utilized to predict an efficacious human dose range of 2000 to 7000 mg.

The first method involved identifying a human dose that would, in the majority of patients (more than 90%), achieve trough lung concentrations (Day 28 after dosing) greater than the concentration that was found to neutralize 90% of the virus (IC90) in vitro. This approach used the human PK as projected from the monkey TK study and incorporated drug distribution into lung tissue (Shah and Betts 2013; Magyarics et al. 2019). This approach identified a dose of 2000 mg.

The second method involved developing a semi-mechanistic SARS-CoV-2 viral dynamic model (Kim et al. 2020) as adapted from a typical viral dynamic model (Cangelosi et al. 2018). This method aimed to identify a dose that would result in the most rapid clearance of virus from a patient and identified a dose of 3000 mg.

The third method was to find a dose that would achieve human serum concentrations throughout a 28-day dosing interval equivalent to serum concentrations in a successful rhesus macaque SARS-CoV-2 challenge study. This method identified that a dose of 7000 mg may be required.

The projected human half-life of LY3832479, based on allometric scaling from monkey data, is expected to be in the 2- to 4-week range.

Safety margins for the proposed starting and maximum dose in this study are shown in Table 4.1.

The proposed starting human dose of 700 mg has a 10-fold margin of safety for evaluation of safety, tolerability, and PK based on expected exposure (AUC) relative to the maximum tested dose in a single-dose monkey toxicity/TK study. The subsequent doses of 2800 and 7000 mg in the single-ascending dose cohorts are planned to be administered following interim safety data from the previous cohorts as described in Section 6.6. The highest proposed dose, 7000 mg, would have a 1x margin of safety. This margin of safety is considered acceptable for the following reasons:

- LY3832479 is a mAb directed against a foreign target and was isolated from a convalescent patient with COVID-19. Therefore, the test article does not bind to antigens/targets expressed in human tissues as confirmed by a GLP-complaint TCR study in human tissues, representing a low risk for potential on-target or off-target toxicity.
- The 1x exposure-based margin for 7000 mg is based on the maximum dose tested in monkeys in the single-dose toxicology/TK study. Based on clinical observations and gross examination at necropsy, no toxicity was observed in the animals administered 186 mg/kg of LY3832479 (final report pending).
- The risk of infusion-related reaction is considered low due to the target, the reduced effector function (Fc and Complement binding), and the human origin of this antibody.
- The engineered LALA mutations are expected to reduce Fc effector function in LY3832479 and should reduce the risk of ADE (see Section 2.2).

Table 4.1. Margin of Safety for Intravenous Administration of LY3832479 Based on Administered Dose and Predicted Exposure

	Dose (mg/kg)	Dose Multiple[a]	AUC0-∞ (mg*h/mL)[a]	AUC Exposure Multiple[a]	Cmax (mg/mL)	Cmax Exposure Multiple[a]
Starting human dose[b]	10	18.6	75	~10	0.253	~19
Highest human dose[b]	100	1.86	753	~1.0	2.51	~1.9
Cynomolgus monkey maximum tested dose[c]	186		750		4.75	

Abbreviations: AUC = area under the concentration versus time curve; AUC0-∞ = AUC from time zero to infinity; Cmax = maximum drug concentration; NOAEL = no-observed-adverse-effect level.

[a] Dose multiple is the dose in animals/dose in humans based on milligrams per kilogram. Exposure multiple is the calculated AUC and Cmax in animals and predicted AUC and Cmax in humans.

[b] Assume 70-kg bodyweight.

[c] Maximum tested dose in the single-dose monkey toxicology/toxicokinetic study.

4.4. End of Study Definition

A participant is considered to have completed the study if he/she has completed all required phases of the study including the last scheduled procedure shown in the Schedule of Activities (SoA).

The end of the study is defined as the date of last scheduled procedure shown in the SoA for the last participant.

5. Study Population

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, *is not permitted.*

5.1. Inclusion Criteria

Participants are eligible to be included in the study only if all of the following criteria apply:

Age

1. are aged 18 to 60 years at the time of signing the informed consent.

Type of Participant and Disease Characteristics

2. are overtly healthy as determined by medical evaluation including medical history and physical examination
3. have safety laboratory test results within the reference range for the population at the study site, or results with acceptable deviations that are judged to be not clinically significant by the investigator
4. have venous access sufficient to allow for blood sampling and IV infusion as described in this protocol (SoA, Section 1.3)
5. are reliable and willing to make themselves available for the duration of the study
6. are willing to follow study procedures, including having nasal or nasopharyngeal swabs collected as described in this protocol (SoA, Section 1.3).

Weight

7. have a BMI within the range $\geq$18.5 to <35 kg/m^2.

Sex

8. are male or female
    a. Male participants must agree to adhere to contraception restrictions
    b. Female participants must be of non-childbearing potential

Contraception requirements and definition of non-childbearing potential are detailed in Appendix 4 (Section 10.4).

Informed Consent

9. are capable of giving signed informed consent as described in Appendix 1, which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol

5.2. Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply:

Medical Conditions

10. have current SARS-CoV-2 infection confirmed by nasal or nasal pharyngeal swab results at screening

11. have had prior SARS-CoV-2 infection, confirmed by either previous nucleic acid-based test, or previous serology
12. have suspected current SARS-CoV-2 infection, in the opinion of the investigator, based on either or both of the following:
    a. a recent exposure to SARS-CoV-2, defined as:
       - living in the same household as a person with SARS-CoV-2
       - having had direct physical contact with a person with SARS-CoV-2 (e.g. shaking hands);
       - having unprotected direct contact with infectious secretions of a person with SARS-CoV-2 (e.g. being coughed on, touching used paper tissues with a bare hand);
       - having had face-to-face contact with a person with SARS-CoV-2, within 2 m and for more than 15 minutes
    b. signs or symptoms that, in the opinion of the investigator, are suggestive of infection (e.g., fever, dry cough, shortness of breath, hypoxia, etc.)
13. have a history or presence of cardiovascular (including hypertension), respiratory, hepatic, renal, gastrointestinal, endocrine, hematological, or neurological disorders that, in the opinion of the investigator, are capable of
    a. significantly altering the absorption, metabolism, or elimination of drugs
    b. constituting a risk while taking the investigational product, or
    c. interfering with the interpretation of data
14. have clinically significant abnormal electrocardiogram (ECG) results constituting a risk while taking the investigational product, as determined by the investigator
15. have an abnormal blood pressure (BP) as determined by the investigator. In case BP appears to be abnormally high during the screening period, it is possible to repeat the measure(s) 1 time in a quiet room to avoid an exclusion due to the white coat effect
16. have significant allergies to humanized mAbs
17. have any of the following that are clinically significant:
    a. multiple or severe drug allergies, or
    b. intolerance to topical corticosteroids, or
    c. severe posttreatment hypersensitivity reactions (including, but not limited to, erythema multiforme major, linear immunoglobulin A dermatosis, toxic epidermal necrolysis, or exfoliative dermatitis)
18. have known allergies to LY3832479, related compounds, or any components of the formulation
19. have had lymphoma, leukemia, or any malignancy within the past 5 years, except for basal cell or squamous epithelial carcinomas of the skin that have been resected with no evidence of metastatic disease for 3 years
20. have had breast cancer within the past 10 years
21. show evidence of human immunodeficiency virus (HIV) infection and/or positive human HIV antibodies
22. show evidence of current hepatitis C (that is, test positive for anti-hepatitis C antibody with confirmed presence of hepatitis C virus [HCV] RNA)

Note: Patients with a previous diagnosis of hepatitis C who received antiviral therapy and achieved a sustained virological response may be eligible for inclusion in the study, provided that they have no detectable HCV RNA on the screening HCV polymerase chain reaction test for this protocol. A sustained virological response is defined as an undetectable HCV RNA level 24 weeks after completion of a full, documented course of an approved antiviral therapy for HCV.
Patients who have spontaneously cleared HCV infection, defined as (1) a positive HCV antibody test and (2) a negative HCV RNA test, with no history of HCV antibody (anti-HCV) treatment, may be eligible for inclusion in the study, provided that they have no detectable HCV RNA at screening for this study.

23. show evidence of current hepatitis B:
    a. test positive for hepatitis B surface antigen, and/or
    b. test positive for hepatitis B core antibody and negative for hepatitis B surface antibody
24. have a significant history of or current psychiatric disorders

Prior/Concomitant Therapy

25. have received treatment with biologic agents (such as mAbs, including marketed drugs) within 3 months or 5 half-lives (whichever is longer) prior to dosing
26. have previously completed or withdrawn from this study and have previously received the investigational product
27. intend to use over-the-counter medication in the 7 days prior to dose administration or prescription medication in the 14 days prior to dose administration, with the exception of hormone replacement therapy, thyroid replacement medications, vitamin and mineral supplements, and occasional use of acetaminophen

Prior/Concurrent Clinical Study Experience

28. are currently enrolled in a clinical study involving an investigational product or any other type of medical research judged not to be scientifically or medically compatible with this study
29. have participated in a clinical study involving an investigational product, with last dose within the past 30 days or 5 half-lives (whichever is longer) prior to dosing

Other Exclusions

30. are pregnant or breast feeding
31. have donated blood of more than 500 mL within the previous 3 months of study screening, or intend to donate blood during the course of the study
32. have an average weekly alcohol intake that exceeds 21 units per week (males) or 14 units per week (females), or are unwilling to stop alcohol consumption from 48 hours prior to admission to and while resident at the clinical research unit (CRU) (1 unit = 12 oz or 360 mL of beer; 5 oz or 150 mL of wine; 1.5 oz or 45 mL of distilled spirits)
33. currently smoke in excess of 10 cigarettes per day or are unwilling to abide by CRU smoking restrictions
34. regularly use known drugs of abuse and/or show positive findings on drug screening unless they were prescribed by a physician (e.g. benzodiazepines).

35. are Lilly employees or are employees of a third-party organization involved with the study that requires exclusion of its employees are study site personnel directly affiliated with this study or their immediate families. Immediate family is defined as a spouse, biological or legal guardian, child, or sibling.
36. in the opinion of the investigator or sponsor, are unsuitable for inclusion in the study.

5.3. Lifestyle Considerations

Reproductive and contraceptive guidance is provided in Section 10.4, Appendix 4.

5.3.1. Meals and Dietary Restrictions

Participants will be required to fast overnight or for at least 4 hours before being given a dose of LY3832479 (see SoA, Section 1.3). Per oral intake should be limited to clear liquids for 4 hours prior to dosing. Standard meals will be administered while participants are resident at the study site.

5.3.2. Caffeine, Alcohol, and Tobacco

Participants must abide by the CRU restriction policy regarding consumption of alcohol and tobacco.

5.3.3. Activity

Participants should not engage in strenuous physical exercise or activities from 48 hours prior to dosing until discharge from the study or completion of all study procedures. When certain study procedures are in progress at the site, participants may be required to remain supine or sitting.

5.4. Screen Failures

Screen failures are defined as participants who consent to participate in the clinical study but are not subsequently enrolled in the study.

Individuals who fulfill eligibility criteria but are not randomized within the 14-day screening window may still enroll in the study provided randomization occurs within 28 days of the first screening visit, and provided that they repeat the nasal or nasopharyngeal swab. These subjects do not need to be documented as screen failures. Subjects who are eligible but are not enrolled within 28 days of their initial screening visit will need to follow re-screen procedures described below.

For the purposes of assessing eligibility, screening clinical laboratory tests may be repeated if the result is considered likely due to a technical or handling error.

Individuals who do not meet the criteria for participation in this study (screen failure) due to a transient minor illness or concomitant medication may be re-screened if and when they later meet eligibility criteria.

Re-screened participants should be assigned a new screening number. When re-screening, all screening tests and procedures should be repeated (except safety laboratory analyses if randomization is to occur within 28 days of the first screening tests). Individuals may be re-screened once, and must sign a new ICF.

6. Study Intervention

Study intervention is defined as any investigational intervention(s) or placebo intended to be administered to a study participant according to the study protocol.

6.1. Study Interventions Administered

Intervention Name	LY3832479	Placebo
Type	Biologic	Not applicable
Dose Formulation	Solution for infusion	0.9% sodium chloride solution
Unit Dose Strength(s)	400-mg vial	Placebo
Dosage Level(s)	• Cohort 1: 700 mg • Cohort 2: 2800 mg • Cohort 3: 7000 mg	Not applicable
Route of Administration	IV infusion	IV infusion
Use	Experimental	Placebo
IMP and NIMP	IMP	IMP
Sourcing	Provided by Lilly	Provided by site
Packaging and Labeling	Provided in glass vials and labeled appropriately	Per site procedure

Abbreviations: IMP = investigational medicinal product; IV = intravenous; NIMP = noninvestigational medicinal product.

This following table describes the infusion volume and rate for LY3832479. Placebo volume and rate will match the LY3832479 dose cohort.

The infusion rate may be reduced as deemed necessary if an infusion reaction is observed. To ensure close monitoring, participants will remain in or close to their bed for at least 6 hours after completion of the infusion.

LY3832479 Dose (mg)	Volume withdraw from DP vial (mL)	Volume of sterile diluent (mL)	Total infusion volume (mL)	Start infusion rate(duration)
700	17.5	32.5	50	100 mL/h (30 min, allowable range 25 - 60 min)
2800	70	None	70	100 mL/h (42 min, allowable range 37 – 75 min)
7000	175	None	175	100 mL/h (105 min, allowable range 100 - 150 min)

6.1.1. Infusions

6.1.1.1. Premedication for Infusions

Premedication for infusions is not planned.

6.1.1.2. Management of Infusion Reactions

All participants should be monitored closely, during and after infusion as specified in the SoA, as there is a risk of infusion reaction and hypersensitivity (including anaphylaxis) with any biological agent.

Symptoms and Signs

Symptoms and signs that may occur as part of an infusion reaction include, but are not limited to fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, and dizziness.

Severity of infusion-related reactions will be assessed and reported using the Division of Allergy and Infectious Diseases (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, version 2.1 (July 2017).

This table describes the severity of reactions according to DAIDS.

Parameter	Mild	Moderate	Severe	Severe and Potentially Life-threatening
Acute Allergic Reaction	Localized urticaria (wheals) with no medical intervention indicated	Localized urticaria with intervention indicated OR Mild angioedema with no intervention indicated	Generalized urticaria OR Angioedema with intervention indicated OR Symptoms of mild bronchospasm	Acute anaphylaxis OR Life-threatening bronchospasm OR Laryngeal edema
Cytokine Release Syndrome[a]	Mild signs and symptoms AND Therapy, that is, antibody infusion interruption not indicated	Therapy indicated (that is, antibody infusion) interruption indicated AND Responds promptly to symptomatic treatment OR Prophylactic medications indicated for ≤24 hours	Prolonged severe signs and symptoms OR Recurrence of symptoms following initial improvement	Life-threatening consequences (for example, requiring pressor or ventilator support)

[a] A disorder characterized by nausea, headache, tachycardia, hypotension, rash, and/or shortness of breath.

Source: Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.1 (July 2017).

Site Needs

The site must have resuscitation equipment, emergency drugs (including but not limited to oxygen, IV fluid, epinephrine, acetaminophen, and antihistamine) and appropriately trained personnel available during the infusion and for at least 6 hours after the completion of the infusion.

Management of Infusion Reactions

Investigators should determine the severity of the infusion reaction and manage infusion reactions based on their clinical judgment and national and international guidance (Lieberman et al 2015; Simons et al. 2015). If an infusion reaction occurs, then supportive care should be used in accordance with the signs and symptoms.

6.1.1.3. Retrospective Positive Sterility Findings from Prepared Study Intervention

If a positive sterility finding occurs in the terminally sterile filtered study intervention, the participants who were dosed from the impacted batch should be contacted immediately and undergo a full physical examination including, but not limited to, BP, pulse rate, and body temperature.

A blood sample should be collected for culture and assayed for inflammatory markers such as C-reactive protein and elevations in white blood cell counts.

If the signs and symptoms indicated a participant has a possible infection, they will be clinically managed, treated, and followed up until resolution. Any AEs will be recorded as appropriate.

6.2. Preparation/Handling/Storage/Accountability

The investigator or designee must confirm appropriate temperature conditions have been maintained during transit for all study interventions received and any discrepancies are reported and resolved before use of the study intervention.

To protect blinding, the interventions must be prepared by unblinded site personnel qualified to prepare study intervention who are not involved in any other study-related procedures. Instructions for preparation will be provided by the sponsor.

Only participants enrolled in the study may receive study intervention and only authorized site personnel may supply or administer study intervention. All study interventions must be stored in a secure, environmentally controlled, and monitored (manual or automated) area in accordance with the labeled storage conditions with access limited to the investigator and authorized site personnel.

The investigator, institution, or the head of the medical institution (where applicable) is responsible for study intervention accountability, reconciliation, and record maintenance (i.e., receipt, reconciliation, and final disposition records).

Further guidance and information for the final disposition of unused study interventions are provided in the pharmacy manual.

6.3. Measures to Minimize Bias: Randomization and Blinding

Randomization tables for allocation of either LY3832479 or placebo will be prepared by the statistician or their designee.

Blinding will be maintained throughout the conduct of the study as described in the separate Blinding Plan.

Emergency codes will be available to the investigator. A code, which reveals the treatment group for a specific study subject, may be opened during the study only if the subject's well-being requires knowledge of the subject's treatment assignment.

In case of an emergency, the investigator has the sole responsibility for determining if unblinding of a subject's treatment assignment is warranted for medical management of the event. The subject's safety must always be the first consideration in making such a determination. If the investigator decides that unblinding is warranted, it is the responsibility of the investigator to promptly document the decision and rationale and notify Lilly as soon as possible.

If an investigator, site personnel performing assessments, or participant is unblinded while the infusion is ongoing, the participant must be discontinued from the study intervention and the infusion stopped. If any amount of study intervention was administered, follow procedures according to the SoA as described in Section 7.1.

Upon completion of the study, all codes must be returned to Lilly or its designee.

6.4. Study Intervention Compliance

Participants will receive study intervention directly from the investigator or designee, under medical supervision. The date and time of each dose administered in the clinic will be recorded in the source documents and recorded in the CRF. The dose of study intervention and study participant identification will be confirmed at the time of dosing by a member of the study site personnel other than the person administering the study intervention.

6.5. Concomitant Therapy

All concomitant medications, whether prescription or over the counter, used at baseline and/or during the course of the trial, must be recorded on the Concomitant Medication electronic case report form (eCRF). Participants will be instructed to consult the investigator or other appropriate study personnel at the study site before taking any new medications or supplements during the study.

In general, concomitant medication should be avoided. Use of chronic, stable doses of hormone replacement therapy, thyroid replacement medications, or vitamin and mineral supplements is allowed. Acetaminophen (1 g, maximum 3 g/24 hours) may be administered at the discretion of the investigator for treatment of headache, etc.

If the need for concomitant medication (other than acetaminophen) arises, inclusion or continuation of the participant may be at the discretion of the investigator after consultation with a Lilly clinical pharmacologist or clinical research physician (CRP).

Any medication used during the course of the study must be documented.

All vaccines are prohibited until study completion.

6.6. Dose Modification

Depending on the results of a given trial-level safety review, the dose of the subsequent cohort(s) may be adjusted. Because these adjustments to dose levels are allowable changes permitted by the protocol, they would not require a protocol amendment.

6.6.1. Dose-Escalation Criteria

By nature of being a Phase 1 sponsor unblinded dose-escalation study, data will be evaluated on an ongoing basis until the highest planned dose has been administered.

After at least 7 participants have completed Day 4 in a given cohort, all safety data up to this cutoff date will be reviewed to determine whether the next cohort can be randomized after agreement between Lilly's medical monitor and the investigator. Safety and tolerability data will be the primary criteria guiding dose escalation.

The investigator and the Lilly sponsor team are responsible for determining any dose decisions. The investigator(s) will remain blinded and the Lilly sponsor team will be unblinded during these reviews. All available data from previous cohorts will be reviewed.

If temporary stopping criteria are met (Section 6.6.3), dosing will be temporarily halted and no further participants will be dosed until a full safety review of the study has taken place.

6.6.2. Access to Data during the Study

A limited number of unblinded Lilly study team personnel will have access to safety and/or PK data during the study.

6.6.3. Temporary Stopping Criteria

Dosing will be temporarily halted, and no further participants will be dosed until safety data available at that point have been reviewed, if

- 3 or more participants develop AEs that are considered to be related to study treatment and graded as at least moderate, clinically significant, and not responsive to supportive care.
- 1 or more participants develop AEs that are considered to be related to study treatment and that are serious (serious adverse events [SAEs]) or graded as severe.

This table describes the location of AE-related information in this protocol.

Topic	Location
DAIDS table describing severity of reactions	Section 6.1.1.2
Definition of AEs	Section 10.3.1
Assessment of Intensity/Severity	Section 10.3.3

Changes to the planned dosing schedule must be appropriately documented and communicated with the study personnel and the institutional review board (IRB)/independent ethics committee (IEC) before dosing continues.

6.7. Intervention after the End of the Study

Not applicable.

7. Discontinuation of Study Intervention and Participant Discontinuation/Withdrawal

These sections describe reasons for a participant's

- permanent or temporary discontinuation of study drug, or
- discontinuation (withdrawal) from the study.

Discontinuation of specific sites or of the trial as a whole are handled as part of regulatory, ethical, and trial oversight considerations in Section 10.1 Appendix 1.

7.1. Discontinuation of Study Intervention

In rare instances, it may be necessary for a participant to permanently discontinue study intervention. If the IV infusion is permanently stopped, the participant will remain in the study for follow-up and further evaluations as described in the SoA.

7.2. Participant Discontinuation/Withdrawal from the Study

A participant may withdraw from the study

- at any time at his/her own request
- at the request of his/her designee (for example, parents or legal guardian)
- at the discretion of the investigator for safety, behavioral, compliance, or administrative reasons
- if the participant becomes pregnant during the study
- if enrollment in any other clinical study involving an investigational product or enrollment in any other type of medical research judged not to be scientifically or medically compatible with this study

At the time of discontinuing from the study, if possible, an early discontinuation visit should be conducted, as shown in the SoA. See SoA for data to be collected at the time of study discontinuation and follow-up and for any further evaluations that need to be completed. The participant will be permanently discontinued both from the study intervention and from the study at that time.

If the participant withdraws consent for disclosure of future information, the sponsor may retain and continue to use any data collected before such a withdrawal of consent. If a participant withdraws from the study, he/she may request destruction of any samples taken and not tested, and the investigator must document this in the site study records.

7.2.1. Discontinuation of Inadvertently Enrolled Participants

If the sponsor or investigator identifies a participant who did not meet enrollment criteria and was inadvertently enrolled, then the participant should be discontinued from study treatment and safety follow-up should be performed as outlined in

- Section 1.3 (SoA),
- Section 8.2 (Safety Assessments), and

- Section 8.3 (Adverse Events and Serious Adverse Events).

7.3. Lost to Follow-up

A participant will be considered lost to follow-up if he or she repeatedly fails to return for scheduled visits and is unable to be contacted by the study site. Site personnel are expected to make diligent attempts to contact participants who fail to return for a scheduled visit or were otherwise unable to be followed up by the site.

8. Study Assessments and Procedures

Study procedures and their timing are summarized in the SoA (Section 1.3).

Immediate safety concerns should be discussed with the sponsor immediately upon occurrence or awareness to determine if the participant should continue or discontinue study intervention.

Adherence to the study design requirements, including those specified in the SoA, is essential and required for study conduct.

All screening evaluations must be completed and reviewed to confirm that potential participants meet all eligibility criteria. The investigator or designee will maintain a screening log to record details of all participants screened and to confirm eligibility or record reasons for screening failure, as applicable.

8.1. Efficacy Assessments

Not applicable.

8.2. Safety Assessments

Planned time points for all safety assessments are provided in the SoA.

8.2.1. Vital Signs

For each participant, vital sign measurements should be conducted according to the SoA (Section 1.3). Additional vital signs may be measured during each study period at the investigator's judgment. Blood pressure and pulse rate should be measured after at least 5 minutes supine.

Orthostatic vital signs should be assessed, if possible, during any AE of dizziness or posture-induced symptoms. If orthostatic measurements are required, participants should be supine for at least 5 minutes and stand for at least 3 minutes. If the participant feels unable to stand, supine vital signs only will be recorded.

Additional vital signs may be measured during each study period if warranted.

8.2.2. Electrocardiograms

Single 12-lead ECG readings will be obtained as outlined in the SoA (see Section 1.3).

Electrocardiograms should be recorded before collecting any blood for safety or PK tests. Subjects must be supine for approximately 5 to 10 minutes before ECG collection and remain supine but awake during ECG collection.

Paper copies of all ECGs recorded should be stored at the investigational site.

Electrocardiograms may be obtained at additional times, when deemed clinically necessary. Collection of additional ECGs at a particular time point is allowed to ensure high-quality records. Electrocardiograms will be interpreted by a qualified physician (the investigator or qualified designee) at the study site as soon after the time of ECG collection as possible, and ideally while the subject is still present, to determine whether the subject meets entry criteria at

the relevant visit(s) and for immediate subject management, should any clinically relevant findings be identified.

Any clinically significant findings from ECGs that result in a diagnosis and that occur after the subject receives the investigational product should be reported to Lilly, or its designee, as an AE via the eCRF.

8.2.3. Clinical Safety Laboratory Assessments

See Section 10.2, Appendix 2 for the list of clinical laboratory tests to be performed and to the SoA for the timing and frequency.

All protocol-required laboratory assessments, as defined in Appendix 2, must be conducted in accordance with the laboratory manual and the SoA.

The investigator must review the laboratory report, document this review, and record any clinically relevant changes occurring during the study in the AE section of the CRF. The laboratory reports must be filed with the source documents.

If laboratory values from nonprotocol-specified laboratory assessments performed at the institution's local laboratory require a change in participant management or are considered clinically significant by the investigator (e.g., SAE or AE or dose modification), then the results must be recorded in the CRF.

8.2.4. Hepatic Monitoring

Close hepatic monitoring

Laboratory tests (Appendix 6, Section 10.6), including ALT, AST, ALP, TBL, D. Bil, GGT, and CK, should be repeated within 48 to 72 hours to confirm the abnormality and to determine if it is increasing or decreasing, if one or more of these conditions occur:

If a participant with baseline results of ...	develops the following elevations:
ALT or AST <1.5x ULN	ALT or AST ≥3x ULN
ALP <1.5x ULN	ALP ≥2x ULN
TBL <1.5x ULN	TBL ≥2x ULN (except for patients with Gilbert's syndrome)
ALT or AST ≥1.5x ULN	ALT or AST ≥2x baseline
ALP ≥1.5x ULN	ALP ≥2x baseline
TBL ≥1.5x ULN	TBL ≥2x baseline (except for patients with Gilbert's syndrome)

If the abnormality persists or worsens, clinical and laboratory monitoring, and evaluation for possible causes of abnormal liver tests should be initiated by the investigator in consultation with the Lilly-designated medical monitor. At a minimum, this evaluation should include physical examination and a thorough medical history, including symptoms, recent illnesses (for example, heart failure, systemic infection, hypotension, or seizures), recent travel, history of concomitant medications (including over-the-counter), herbal and dietary supplements, history of alcohol drinking and other substance abuse.

Initially, monitoring of symptoms and hepatic biochemical tests should be done at a frequency of 1 to 3 times weekly, based on the participant's clinical condition and hepatic biochemical tests. Subsequently, the frequency of monitoring may be lowered to once every 1 to 2 weeks, if the participant's clinical condition and lab results stabilize. Monitoring of ALT, AST, ALP, and TBL should continue until levels normalize or return to approximate baseline levels.

Comprehensive hepatic evaluation

A comprehensive evaluation should be performed to search for possible causes of liver injury if one or more of these conditions occur:

If a participant with baseline results of...	develops the following elevations:
ALT or AST <1.5x ULN	ALT or AST ≥3x ULN with hepatic signs/symptoms*, or ALT or AST ≥5x ULN
ALP <1.5x ULN	ALP ≥3x ULN
TBL <1.5x ULN	TBL ≥2x ULN (except for patients with Gilbert's syndrome)
ALT or AST ≥1.5x ULN	ALT or AST ≥2x baseline with hepatic signs/symptoms*, or ALT or AST ≥3x baseline
ALP ≥1.5x ULN	ALP ≥2x baseline
TBL ≥1.5x ULN	TBL ≥1.5x baseline (except for patients with Gilbert's syndrome)

* Hepatic signs/symptoms are severe fatigue, nausea, vomiting, right upper quadrant abdominal pain, fever, rash, and/or eosinophilia >5%.

At a minimum, this evaluation should include physical examination and a thorough medical history, as outlined above, as well as tests for PT-INR; tests for viral hepatitis A, B, C, or E; tests for autoimmune hepatitis; and an abdominal imaging study (for example, ultrasound or CT scan).

Based on the patient's history and initial results, further testing should be considered in consultation with the Lilly-designated medical monitor, including tests for hepatitis D virus (HDV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), acetaminophen levels, acetaminophen protein adducts, urine toxicology screen, Wilson's disease, blood alcohol levels, urinary ethyl glucuronide, and serum phosphatidylethanol. Based on the circumstances and the investigator's assessment of the participant's clinical condition, the investigator should consider referring the participant for a hepatologist or gastroenterologist consultation, magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), cardiac echocardiogram, or a liver biopsy.

Additional hepatic data collection (hepatic safety CRF) in study participants who have abnormal liver tests during the study

Additional hepatic safety data collection in hepatic safety case report forms (CRF) should be performed in study participants who meet 1 or more of the following 5 conditions:

1. Elevation of serum ALT to ≥5x ULN on 2 or more consecutive blood tests (if baseline ALT <1.5x ULN)
    - In participants with baseline ALT ≥1.5x ULN, the threshold is ALT ≥3x baseline on 2 or more consecutive tests
2. Elevated TBL to ≥ 2x ULN (if baseline TBL <1.5x ULN) (except for cases of known Gilbert's syndrome)
    - In participants with baseline TBL ≥1.5x ULN, the threshold should be TBL ≥2x baseline
3. Elevation of serum ALP to ≥2x ULN on 2 or more consecutive blood tests (if baseline ALP <1.5x ULN)
    - In participants with baseline ALP ≥1.5x ULN, the threshold is ALP ≥2x baseline on 2 or more consecutive blood tests
4. Hepatic event considered to be a serious adverse event (SAE)
5. Discontinuation of study drug due to a hepatic event.

Note: the interval between the two consecutive blood tests should be at least 2 days.

8.3. Adverse Events and Serious Adverse Events

Adverse events will be reported by the participant.

The investigator and any qualified designees are responsible for detecting, documenting, and recording events that meet the definition of an AE or SAE and remain responsible for following up AEs that are serious, considered related to the study intervention or study procedures, or that caused the participant to discontinue the study intervention or study.

Discontinuation information is in Section 7.

Detailed AE definitions and procedures are in Section 10.3.

8.3.1. Time Period and Frequency for Collecting AE and SAE Information

All AEs and SAEs will be collected from the time of signing of the ICF until participation in the study has ended.

Adverse events that begin before the start of study intervention but after signing of the ICF will be recorded on the Adverse Event CRF.

Although all AEs after signing the ICF are recorded by the site in the CRF/electronic data entry, SAE reporting to sponsor begins after the participant has signed the ICF and has received study intervention. However, if an SAE occurs after signing the ICF, but prior to receiving study intervention, it needs to be reported within the SAE reporting time frame if it is considered reasonably possibly related to study procedures.

All SAEs will be recorded and reported to the sponsor or designee immediately and under no circumstance should this exceed 24 hours, as indicated in Section 10.3, Appendix 3. The investigator will submit any updated SAE data to the sponsor within 24 hours of it being available.

Investigators are not obligated to actively seek AEs or SAEs after conclusion of the study participation. However, if the investigator learns of any SAE, including a death, at any time after a participant has been discharged from the study, and he/she considers the event to be reasonably related to the study intervention or study participation, the investigator must promptly notify the sponsor.

8.3.2. Method of Detecting AEs and SAEs

The method of recording, evaluating, and assessing causality of AE and SAE and the procedures for completing and transmitting SAE reports are provided in Section 10.3.

Care will be taken not to introduce bias while detecting AEs and/or SAEs. Open-ended and nonleading verbal questioning of the participant is the preferred method to inquire about AE occurrences.

8.3.3. Follow-up of AEs and SAEs

After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs will be followed up until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3). Further information on follow-up procedures is provided in Section 10.3.

8.3.4. Regulatory Reporting Requirements for SAEs

Prompt notification by the investigator to the sponsor of an SAE is essential so that legal obligations and ethical responsibilities toward the safety of participants and the safety of a study intervention under clinical investigation are met.

The sponsor has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study intervention under clinical investigation. The sponsor will comply with country-specific regulatory requirements relating to safety reporting to the regulatory authority, IRB/IEC, and investigators.

An investigator who receives an investigator safety report describing an SAE or other specific safety information (e.g., summary or listing of SAEs) from the sponsor will review and then file it with the IB, and will notify the IRB/IEC, if appropriate according to local requirements.

8.3.5. Pregnancy

Details of all pregnancies in female participants and female partners of male participants will be collected after the start of study intervention and until at least 5 months after the last dose.

If a pregnancy is reported, the investigator should inform the sponsor within 24 hours of learning of the pregnancy and should follow the procedures outlined in Section 10.4.

Abnormal pregnancy outcomes (e.g., spontaneous abortion, fetal death, stillbirth, congenital anomalies, ectopic pregnancy) are considered SAEs.

8.3.6. Hypersensitivity Reactions

Many drugs, but particularly biologic agents, carry the risk of systemic hypersensitivity reactions. If such a reaction occurs, additional details describing each symptom should be provided to the sponsor in the infusion-related reaction/hypersensitivity CRF.

If symptoms and/or signs occur during or within 6 hours after end of infusion of LY3832479 and are believed to be hypersensitivity or due to cytokine release, then investigators are encouraged to report the event as infusion-related immediate hypersensitivity reaction or cytokine release-associated infusion reaction, respectively.

Sites should have appropriately trained medical personnel and appropriate medical equipment available when study participants are receiving intervention. It is recommended that participants who experience a systemic hypersensitivity reaction be treated per national and international guidance (Lieberman et al 2015; Simons et al. 2015)

In the case of generalized urticaria or anaphylaxis, additional blood and urine samples should be collected as described in Section 10.7, Appendix 7, "Recommended Laboratory Testing for Hypersensitivity Events". Laboratory results are provided to the sponsor via the central laboratory.

8.3.7. SARS-COV-2 Infection

In the event of a suspected SARS-CoV-2 infection, participants will undergo a viral test using nasal or nasopharyngeal swab and be managed according to standard of care.

Suspicion of SARS-CoV-2 infection, in the opinion of the investigator, will rely upon

- a recent exposure to SARS-CoV-2 defined as:
  - living in the same household as a person with SARS-CoV-2;
  - having had direct physical contact with a person with SARS-CoV-2 (e.g. shaking hands);
  - having unprotected direct contact with infectious secretions of a person with SARS-CoV-2 (e.g. being coughed on, touching used paper tissues with a bare hand);
  - having had face-to-face contact with a person with SARS-CoV-2, within 2 m and for more than 15 minutes.
- and/or signs or symptoms that, in the opinion of the investigator, are suggestive of SARS-CoV-2 infection (e.g., fever, dry cough, shortness of breath, hypoxia, etc.)

In addition, SARS-CoV-2 point-of-care tests may be performed at specific timepoints during the study at the discretion of the investigator. Every time such a point-of-care test is performed post baseline, an additional nasal or nasopharyngeal swab sample may be collected in parallel, for research purposes such as viral sequencing. This research swab sample will be shipped to the sponsor only if the point-of-care test is positive. If the point-of-care test is negative, the research swab sample should be discarded.

If any participant is tested positive post baseline, prior to this protocol amendment being approved, an additional nasal or nasopharyngeal swab sample may be collected for research purposes.

8.3.8. Infusion-Related Reactions

As with other mAbs, infusion-related reactions may occur during or following LY3832479 administration. If an infusion-related reaction occurs, additional data describing each symptom and sign should be provided to the sponsor in the CRF.

This table describes the location of infusion-related reaction information in this protocol.

Topic	Location
Special treatment considerations	Section 6.1.1
Management of infusion reactions	Section 6.1.1.2
DAIDS table describing severity	Section 6.1.1.2
Treatment guidelines for infusion-related reactions	Section 6.1.1.2

Symptoms occurring during or after infusion of study intervention may also be defined according to AE categories such as acute allergic reaction or cytokine release syndrome (refer to DAIDS).

8.3.9. Product Complaints

A product complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a trial intervention.

The sponsor collects product complaints on study interventions used in clinical studies to ensure the safety of study participants, monitor quality, and to facilitate process and product improvements.

Participants will be instructed to contact the investigator as soon as possible if they have a complaint or problem with the study intervention so that the situation can be assessed.

NOTE: Any AEs or SAEs that are associated with a product complaint will follow the processes outlined in Section 8.3.3 and Appendix 10.3 of the protocol.

Time Period for Detecting Product Complaints

Product complaints that result in an AE will be detected, documented, and reported to the sponsor during all periods of the study in which the study intervention is used.

If the investigator learns of any product complaint at any time after a participant has been discharged from the study, and such incident is considered reasonably related to the study intervention, the investigator will promptly notify the sponsor.

Prompt Reporting of Product Complaints to Sponsor

Product complaints will be reported to the sponsor within 24 hours after the investigator becomes aware of the complaint.

The Product Complaint Form will be sent to the sponsor by a method designated by the sponsor.

Follow-up of Product Complaints

Follow-up applies to all participants, including those who discontinue study intervention.

The investigator is responsible for ensuring that follow-up includes any supplemental investigations as indicated to elucidate the nature and/or causality of the product complaint.

New or updated information will be recorded on the originally completed form with all changes signed and dated by the investigator and submitted to the sponsor.

8.4. Treatment of Overdose

For the purposes of this study, an overdose of LY3832479 is considered any dose higher than the dose assigned through randomization. In case of suspected overdose, participants should be monitored for any signs or symptoms of adverse reactions or effects, and supportive care should be provided as necessary.

8.5. Pharmacokinetics

Venous blood samples will be collected as specified in the SoA for determination of serum concentrations of LY3832479 used to evaluate the PK for LY3832479.

A maximum of 5 samples may be collected at additional time points during the study if warranted and agreed upon between the investigator and the sponsor.

Instructions for the collection and handling of biological samples will be provided by Lilly.

Site personnel will record

- the date and time (24-hour clock time) of administration (start and end of infusion), and
- the date and time (24-hour clock time) of each PK sample.

It is essential that the times are recorded accurately.

8.6. Pharmacodynamics

Pharmacodynamic parameters are not evaluated in this study.

8.7. Genetics

A whole blood sample will be collected for pharmacogenetic analysis where local regulations allow.

See Section 10.2 Clinical Laboratory Tests, and Section 1.3 SoA for sample collection information.

See Section 10.5 for genetic research, custody, and sample retention information.

8.8. Biomarkers

Blood samples will be collected from all participants for analysis of immune system and LY3832479-related markers. Serum samples for exploratory biomarker research will be collected at the time specified in the SoA where local regulations allow.

Samples will be stored and analysis may be performed on biomarkers thought to play a role in immune system-related responses to viral infection or administration of LY3832479 including, but not limited to, immune pathways or serum analytes to evaluate their association with LY3832479 administration.

Samples may be used for research to develop methods, assays, prognostics, and/or companion diagnostics related to the intervention target (S protein), pathways associated with disease, and/or the mechanism of action of the study intervention.

Post-baseline swab samples may be used for research purposes, such as viral sequencing.

Sample retention is described in Section 10.1.10.

8.9. Immunogenicity Assessments

Visits and times

At the visits and times specified in the SoA, predose venous blood samples will be collected to determine antibody production against LY3832479. The actual date and time (24-hour clock time) of each sample collection will be recorded. To aid interpretation of these results, PK samples will be collected at the same time points as the immunogenicity samples.

Sample collection, handling, and use

Instructions for the collection and handling of blood samples will be provided by the sponsor.

Immunogenicity will be assessed using a validated assay designed to detect ADAs in the presence of LY3832479 at a laboratory approved by the sponsor. Antibodies may be further characterized for their ability to neutralize the activity of LY3832479.

Sample retention

Sample retention is described in Section 10.1.10.

8.10. Health Economics

Not applicable.

9. Statistical Considerations

9.1. Statistical Hypotheses

This is an exploratory study with a primary objective of assessing safety and tolerability. Any hypothesis tests conducted for treatment comparisons will be exploratory in nature and conducted without adjustment for multiplicity.

9.2. Sample Size Determination

A maximum of 30 participants will be enrolled to study intervention such that approximately 8 participants have sufficient evaluable data in each cohort.

The sample size is customary for first-in-human studies evaluating safety and PK, and is not powered on the basis of statistical hypothesis testing.

For replacement of participants who are randomized but not dosed, see Section 4.1.1.

9.3. Populations for Analyses

The following populations are defined:

Population	Description
Entered	All participants who sign the ICF
Safety	All participants randomly assigned to study intervention and who are administered at least 1 dose of study intervention. Participants will be analyzed according to the intervention they actually received.
Pharmacokinetic Analysis	All randomized participants who received study intervention and have baseline and have multiple evaluable PK samples.

9.4. Statistical Analyses

Statistical analysis of this study will be the responsibility of sponsor or its designee.

All tests of treatment effects will be conducted at a 2-sided alpha level of 0.05, unless otherwise stated, and all confidence intervals will be given at a 2-sided 95% level.

Any change to the data analysis methods described in the protocol will require an amendment only if it changes a principal feature of the protocol. Any other change to the data analysis methods described in the protocol, and the justification for making the change, will be described in the statistical analysis plan (SAP) and the clinical study report. Additional exploratory analyses of the data will be conducted as deemed appropriate.

The SAP will be finalized prior to unblinding and it will include a more technical and detailed description of the statistical analyses described in this section. This section is a summary of the planned statistical analyses of the most important endpoints including primary and key secondary endpoints.

9.4.1. General Considerations

Statistical analyses will be performed using SAS® Version 9.4 or higher.

For continuous measures, summary statistics will include sample size, mean, standard deviation, minimum, median, and maximum. For categorical measures, summary statistics will include the sample size, frequency count, and percentage.

For all safety analyses, baseline will be defined as the last evaluable value before dosing.

9.4.2. Primary Endpoints (Safety)

All analyses of primary endpoints will be made on the Safety Population.

All investigational product- and protocol procedure-related AEs will be listed and, if the frequency of events allows, safety data will be summarized using descriptive methodology. The incidence of symptoms for each treatment will be presented by severity and by association with investigational product as perceived by the investigator.

A TEAE is defined as an event that emerges after treatment (ie, after administration of placebo or LY3832479), having been absent pretreatment, or worsens relative to the pretreatment state.

The number of participants who experience a TEAE and/or an SAE (all causalities and related to study drug) will be summarized by study treatment. All TEAEs will be summarized by system organ class and by decreasing frequency within system organ class.

Other safety parameters that will be assessed include safety laboratory parameters, vital signs, and ECG parameters. The parameters will be listed and summarized using summary statistics. Additional analysis will be performed if warranted upon review of the data.

9.4.3. Secondary Endpoints (PK)

Pharmacokinetic parameter estimates for LY3832479 will be calculated using standard noncompartmental methods of analysis and summarized by dose using descriptive statistics, if sufficient data are available.

The parameters for analysis will be Cmax and AUC of LY3832479. Other noncompartmental parameters, such as time to Cmax, apparent terminal elimination half-life, clearance, and volume of distribution may be reported. Analyses of other PK parameters may be performed, if appropriate.

A compartmental analysis may also be performed to further characterize LY3832479 PK and support model-based PK simulations.

9.4.4. Tertiary/Exploratory Endpoint (Immunogenicity)

The frequency and percentage of participants with preexisting ADA and treatment-emergent (TE) ADA+ to LY3832479 will be tabulated. Treatment-emergent ADA+ is defined as those with a titer 2-fold (1 dilution) greater than the minimum required dilution if no ADAs were detected at baseline (treatment-induced ADA) or those with a 4-fold (2 dilutions) increase in titer compared to baseline if ADAs were detected at baseline (treatment-boosted ADA). For the TE ADA+ participants, the distribution of maximum titers will be described. The frequency of neutralizing antibodies may also be tabulated in ADA+ participants.

The relationship between the presence of antibodies to LY3832479 concentrations/PK parameters, and/or safety assessment may be assessed.

9.4.5. Other Analyses

9.4.5.1. Participant Disposition

A detailed description of All participants who discontinue from the study will be identified, and the extent of their participation in the study will be reported. If known, a reason for their discontinuation will be given.

9.4.5.2. Participant Characteristics

Each participant's baseline characteristics and other demographic characteristics will be recorded, listed, and summarized by treatment group and overall.

9.5. Interim Analyses

There are no interim analyses planned for this study. If an unplanned interim analysis is deemed necessary, the Lilly CP, CRP/investigator, or designee will consult with the appropriate medical director or designee to determine if it is necessary to amend the protocol.

For details of access to data during the study, see Section 6.6.2.

10. Supporting Documentation and Operational Considerations

10.1. Appendix 1: Regulatory, Ethical, and Study Oversight Considerations

10.1.1. Regulatory and Ethical Considerations

This study will be conducted in accordance with the protocol and with the following:

- Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines
- Applicable International Council for Harmonisation (ICH) good clinical practice (GCP) Guidelines, and
- Applicable laws and regulations.

The protocol, protocol amendments, ICF, IB, and other relevant documents (e.g., advertisements) must be submitted to an IRB/IEC by the investigator and reviewed and approved by the IRB/IEC before the study is initiated.

Any amendments to the protocol will require IRB/IEC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants.

The investigator will be responsible for the following:

- Providing written summaries of the status of the study to the IRB/IEC annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB/IEC
- Notifying the IRB/IEC of SAEs or other significant safety findings as required by IRB/IEC procedures, and
- Providing oversight of the conduct of the study at the site and adherence to requirements of 21 Code of Federal Regulations (CFR), ICH guidelines, the IRB/IEC, and all other applicable local regulations.

Study sites are compensated for participation in the study as detailed in the clinical trial agreement.

10.1.2. Informed Consent Process

The investigator or their representative will explain the nature of the study, including the risks and benefits, to the participant or their legally authorized representative and answer all questions regarding the study.

Participants must be informed that their participation is voluntary. Participants or their legally authorized representative will be required to sign a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act requirements, where applicable, and the IRB/IEC or study center.

The medical record must include a statement that written informed consent was obtained before the participant was entered in the study and the date the written consent was obtained. The authorized person obtaining the informed consent and, if applicable, the individual designated to witness a verbal consent, must also sign the ICF.

Participants must be re-consented to the most current version of the ICF(s) during their participation in the study.

A copy of the ICF(s) must be provided to the participant or the participant's legally authorized representative and is kept on file.

10.1.3. Data Protection

Participants will be assigned a unique identifier by the sponsor. Any participant records, datasets or tissue samples that are transferred to the sponsor will contain the identifier only; participant names or any information that would make the participant identifiable will not be transferred.

The participant must be informed that their personal study-related data will be used by the sponsor in accordance with local data protection law. The level of disclosure must also be explained to the participant who will be required to give consent for their data to be used as described in the informed consent.

The participant must be informed that their medical records may be examined by Clinical Quality Assurance auditors or other authorized personnel appointed by the sponsor, by appropriate IRB/IEC members, and by inspectors from regulatory authorities.

The sponsor has processes in place to ensure data protection, information security, and data integrity. These processes include appropriate contingency plan(s) for appropriate and timely response in the event of a data security breach.

10.1.4. Dissemination of Clinical Study Data

A clinical study report will be provided for this study and a summary of study information provided on publicly available websites.

10.1.5. Data Quality Assurance

Investigator responsibilities

All participant data relating to the study will be recorded on printed or electronic CRF unless transmitted to the sponsor or designee electronically (e.g., laboratory data). The investigator is responsible for verifying that data entries are accurate and correct by physically or electronically signing the CRF.

The investigator must maintain accurate documentation (source data) that supports the information entered in the CRF. Source data may include laboratory tests, medical records, and clinical notes.

The investigator must permit study-related monitoring, audits, IRB/IEC review, and regulatory agency inspections and provide direct access to source data documents.

Data monitoring and management

The Monitoring Plan includes

- monitoring details describing strategy, for example, risk-based initiatives in operations and quality such as risk management and mitigation strategies and analytical risk-based monitoring
- methods
- responsibilities
- requirements
- handling of noncompliance issues, and
- monitoring techniques.

The sponsor or designee is responsible for the data management of this study including quality checking of the data. The sponsor assumes accountability for actions delegated to other individuals (e.g., contract research organizations).

Study monitors will perform ongoing source data verification to confirm that data entered in the CRF by authorized site personnel are accurate, complete, and verifiable from source documents. They will also ensure that the safety and rights of participants are being protected, and that the study is being conducted in accordance with the currently approved protocol and any other study agreements, ICH GCP, and all applicable regulatory requirements.

Records retention and audits

Records and documents, including signed ICFs, pertaining to the conduct of this study must be retained by the investigator for the time period outlined in the clinical trial agreement unless local regulations or institutional policies require a longer retention period.

No records may be destroyed during the retention period without the written approval of the sponsor. No records may be transferred to another location or party without written notification to the sponsor.

The sponsor or its representatives will periodically check a sample of the participant data recorded against source documents at the study site. The study may be audited by the sponsor or its representatives, and by regulatory agencies at any time. Investigators will be given notice before an audit occurs.

Data Capture System

The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor.

An electronic data capture (EDC) system will be used in this study for the collection of CRF data. The investigator maintains a separate source for the data entered by the investigator or designee into the sponsor-provided EDC system. The investigator is responsible for the identification of any data to be considered source and for the confirmation that data reported are accurate and complete by signing the CRF.

Data collected via the sponsor-provided data capture systems will be stored at third parties. The investigator will have continuous access to the data during the study and until decommissioning of the data capture systems. Prior to decommissioning, the investigator will receive an archival copy of pertinent data for retention.

Data managed by a central vendor, such as laboratory test data, will be stored electronically in the central vendor's database system and reports will be provided to the investigator for review and retention. Data will subsequently be transferred from the central vendor to the sponsor data warehouse.

Data from complaint forms submitted to the sponsor will be encoded and stored in the global product complaint management system.

10.1.6. Source Documents

Source documents provide evidence for the existence of the participant and substantiate the integrity of the data collected. Source documents are filed at the investigator's site.

Data reported on the CRF that are transcribed from source documents must be consistent with the source documents or the discrepancies must be explained. The investigator may need to request previous medical records or transfer records, depending on the study. Current medical records must be available.

The definition of what constitutes source data can be found in Section 10.1.5.

10.1.7. Study and Site Start and Closure

The study start date is the date on which the clinical study will be open for recruitment of participants.

Site Closure

The sponsor designee reserves the right to close the study site or terminate the study at any time for any reason at the sole discretion of the sponsor. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The investigator may initiate study-site closure at any time, provided there is reasonable cause and enough notice is given in advance of the intended termination.

Reasons for the early closure of a study site by the sponsor or investigator may include but are not limited to

- failure of the investigator to comply with the protocol, the requirements of the IRB/IEC or local health authorities, the sponsor's procedures, or GCP guidelines
- inadequate recruitment of participants by the investigator, or
- discontinuation of further study intervention development.

If the study is prematurely terminated or suspended, the sponsor shall promptly inform the investigators, the IECs/IRBs, the regulatory authorities, and any contract research organization(s) used in the study of the reason for termination or suspension, as specified by the applicable regulatory requirements. The investigator shall promptly inform the participants and assure appropriate participant therapy and/or follow-up.

10.1.8. Publication Policy

In accordance with the sponsor's publication policy, the results of this study will be submitted for publication by a peer-reviewed journal if the results are deemed to be of significant medical importance.

10.1.9. Investigator Information

Physicians with a specialty in infectious disease, critical care, or pulmonary disease may participate as investigators.

10.1.10. Long-Term Sample Retention

Sample retention enables use of new technologies, response to regulatory questions, and investigation of variable response that may not be observed until later in the development of the intervention or after the intervention becomes commercially available.

This table describes the retention period for potential sample types.

Sample Type	Custodian	Retention Period after Last Participant Visit
Pharmacogenetics sample	Sponsor or designee	up to 15 years
Exploratory Biomarker Samples	Sponsor or designee	up to 15 years
Pharmacokinetic (PK) sample	Sponsor or designee	up to 2 years
Immunogenicity (ADA) sample	Sponsor or designee	up to 15 years

10.2. Appendix 2: Clinical Laboratory Tests

Clinical laboratory tests will be performed according to the SoA. Additional details are provided in the following table for specific laboratory tests.

Additional tests may be performed at any time during the study as determined necessary by the investigator or required by local regulations.

Pregnancy testing will be performed according to the SoA.

The following table describes when the local or central laboratory will be used.

If the local laboratory results are used to make either a study intervention decision or response evaluation, the results must be recorded in the CRF.

Laboratory results that could unblind the study will not be reported to study sites or other blinded personnel.

Protocol-specific requirements for inclusion or exclusion of participants are detailed in Section 5 of the protocol.

Investigators must document their review of each laboratory safety report.

Refer to Section 10.6 for recommended laboratory testing for hypersensitivity events.

Clinical Laboratory Tests	Comments
Hematology	Assayed by local laboratory
Hemoglobin	
Hematocrit	
Erythrocyte count (RBCs - red blood cells)	
Mean cell volume	
Mean cell hemoglobin	
Leukocytes (WBCs - white blood cells)	
Differential	
Neutrophils, segmented	
Lymphocytes	
Monocytes	
Eosinophils	
Basophils	
Platelets	
Cell morphology (RBC and WBC)	
Clinical Chemistry	Assayed by local laboratory
Sodium	
Potassium	
Chloride	
Bicarbonate	
Total bilirubin	
Direct bilirubin	Record on Day 1 and repeat if significantly abnormal value
Alkaline phosphatase (ALP)	
Alanine aminotransferase (ALT)	

Clinical Laboratory Tests	Comments
Aspartate aminotransferase (AST)	
Gamma-glutamyl transferase (GGT)	Record on Day 1 and repeat if significantly abnormal value
Blood urea nitrogen (BUN)	
Creatinine	
Creatine kinase (CK)	Record on Day 1 and repeat if significantly abnormal value
Uric acid	Record on Day 1 and repeat if significantly abnormal value
Total protein	
Albumin	
Calcium	
Phosphorus	
Random glucose	
Calculations	Completed locally
eGFR	Calculated by CKD-EPI equation
Hepatitis B surface antigen	
Hepatitis B core antibody (HBcAb)	
Hepatitis C antibody	
HIV	
SARS-Cov-2 viral infection determination	Local laboratory
SARS-Cov-2 nasopharyngeal test	At screening visit. To be performed only if SARS-CoV-2 point of care test is not available
SARS-Cov-2 point of care	On Day -1 if available, and during the study at the investigator's discretion
SARS-Cov-2 nasal or nasopharyngeal sample for research purposes	Sent to the sponsor for analysis if the SARS-Cov-2 point of care test performed in parallel is positive
SARS-Cov-2 serology	**At screening, and then according to schedule of activities**
Urinalysis	Assayed by local laboratory
Specific gravity	
pH	
Protein	
Glucose	
Ketones	
Bilirubin	
Urobilinogen	
Blood	
Nitrite	
Microscopy	If dipstick test is abnormal.
Hormones (female)	Assayed by local laboratory.
Serum pregnancy	
Urine pregnancy	
Ethanol/drug screening	Assayed by local laboratory.
Urine or breath ethanol screen	
Urine drug screen	
Pharmacokinetic (PK) Samples	Assayed by Lilly-designated laboratory. Results will not be provided to the study sites.

Clinical Laboratory Tests	Comments
Pharmacogenetic sample	Assayed by Lilly-designated laboratory. Results will not be provided to the study sites.
Exploratory Biomarker Samples	Assayed by Lilly-designated laboratory. Results will not be provided to the study sites.
Serum	
Immunogenicity Samples	Assayed by Lilly-designated laboratory. Results will not be provided to the study sites.
Anti-LY3832479 antibodies	
Anti-LY3832479 antibodies neutralization	

Abbreviations: CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; eGFR = estimated glomerular filtration rate; HIV = human immunodeficiency virus; SARS-Cov-2 = severe acute respiratory syndrome coronavirus 2.

10.2.1. Blood Sampling Summary

This table summarizes the approximate number of venipunctures and volumes for all blood sampling during the study.

Protocol J2Z-MC-PGAA Sampling Summary

Purpose	Blood Volume per Sample (mL)	Number of Blood Samples	Total Volume (mL)
Screening tests[a]	45	1	45
Clinical laboratory tests[a]	15	9	135
SARS-CoV-2 serology	10	5	50
Pharmacokinetics (including up to 5 extra samples if needed)	4	11 (16)	44 (64)
Blood discard for cannula patency	1	8	8
Immunogenicity	10	5	50
Pharmacogenetics	3	1	3
Serum for exploratory biomarkers	10	6	60
Total			395 (415)
Total for clinical purposes (rounded up to the nearest 10 mL)			400 (420)

[a] Additional samples may be drawn if needed for safety purposes.

10.3. Appendix 3: Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting

10.3.1. Definition of AE

AE Definition

- An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention.
- NOTE: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study intervention.

Events Meeting the AE Definition

- Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (e.g., ECG, radiological scans, vital sign measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator (i.e., not related to progression of underlying disease).
- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.
- New conditions detected or diagnosed after study intervention administration even though it may have been present before the start of the study.
- Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either study intervention or a concomitant medication. Overdose per se will not be reported as an AE/SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdose should be reported regardless of sequelae.

Events NOT Meeting the AE Definition

- Any clinically significant abnormal laboratory findings or other abnormal safety assessments that are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition.
- The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the participant's condition.
- Medical or surgical procedure (e.g., endoscopy, appendectomy): the condition that leads to the procedure is the AE.
- Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).

- Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the study that do not worsen.

10.3.2. Definition of SAE

If an event is not an AE per definition above, then it cannot be an SAE even if serious conditions are met (e.g., hospitalization for signs/symptoms of the disease under study, death due to progression of disease).

An SAE is defined as any untoward medical occurrence that, at any dose:

a. Results in death

b. Is life-threatening

The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe.

c. Requires inpatient hospitalization or prolongation of existing hospitalization

- In general, hospitalization signifies that the participant has been admitted to hospital for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE should be considered serious.
- Hospitalization for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an AE.

d. Results in persistent disability/incapacity

- The term disability means a substantial disruption of a person's ability to conduct normal life functions.
- This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle) that may interfere with or prevent everyday life functions but do not constitute a substantial disruption.

e. Is a congenital anomaly/birth defect

f. Other situations:

- Medical or scientific judgment should be exercised in deciding whether SAE reporting is appropriate in other situations such as important medical events that may not be immediately life threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention to prevent 1 of the other

outcomes listed in the above definition. These events should usually be considered serious.

- Examples of such events include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias, or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

10.3.3. Recording and Follow-Up of AE and/or SAE

AE and SAE Recording

- When an AE/SAE occurs, it is the responsibility of the investigator to review all documentation (e.g., hospital progress notes, laboratory reports, and diagnostics reports) related to the event.
- The investigator will then record all relevant AE/SAE information in the CRF.
- It is **not** acceptable for the investigator to send photocopies of the participant's medical records to the sponsor or designee in lieu of completion of the AE/SAE CRF page.
- There may be instances when copies of medical records for certain cases are requested by the sponsor or designee. In this case, all participant identifiers, with the exception of the participant number, will be redacted on the copies of the medical records before submission to the sponsor or designee.
- The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE/SAE.

Assessment of Intensity

The investigator will make an assessment of intensity for each AE and SAE reported during the study and assign it to 1 of the following categories:

- Mild: An event that is easily tolerated by the participant, causing minimal discomfort, and not interfering with everyday activities.
- Moderate: An event that causes sufficient discomfort and interferes with normal everyday activities.
- Severe: An event that prevents normal everyday activities. An AE that is assessed as severe should not be confused with an SAE. Severe is a category utilized for rating the intensity of an event; and both AEs and SAEs can be assessed as severe.

  An event is defined as 'serious' when it meets at least 1 of the predefined outcomes as described in the definition of an SAE, NOT when it is rated as severe.

Assessment of Causality

- The investigator is obligated to assess the relationship between study intervention and each occurrence of each AE/SAE.

- The investigator will consider any AEs, SAEs, and clinically important laboratory abnormalities as related to the study intervention unless there is clear evidence that the event is not related.
- The investigator will use clinical judgment to determine the relationship.
- Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study intervention administration will be considered and investigated.
- The investigator will also consult the IB and/or Product Information, for marketed products, in his/her assessment.
- For each AE/SAE, the investigator **must** document in the medical notes that he/she has reviewed the AE/SAE and has provided an assessment of causality.
- There may be situations in which an SAE has occurred and the investigator has minimal information to include in the initial report to the sponsor or designee. However, it is very important that the investigator always make an assessment of causality for every event before the initial transmission of the SAE data to the sponsor or designee.
- The investigator may change his/her opinion of causality in light of follow-up information and send an SAE follow-up report with the updated causality assessment.
- The causality assessment is 1 of the criteria used when determining regulatory reporting requirements.

Follow-up of AEs and SAEs

- The investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as medically indicated or as requested by the sponsor or designee to elucidate the nature and/or causality of the AE or SAE as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals.
- If a participant dies during participation in the study or during a recognized follow-up period, the investigator will provide the sponsor or designee with a copy of any postmortem findings including histopathology.
- New or updated information will be recorded in the originally completed CRF.
- The investigator will submit any updated SAE data to the sponsor or designee within 24 hours of receipt of the information.

10.3.4. Reporting of SAEs

SAE Reporting via Paper CRF

- Facsimile transmission of the SAE Report is the preferred method to transmit this information to the sponsor or designee.
- Initial notification via telephone does not replace the need for the investigator to complete and sign the SAE Report within the designated reporting time frames.

- Contacts for SAE reporting can be found in the SAE Report.

10.4. Appendix 4: Contraceptive Guidance and Collection of Pregnancy Information

10.4.1. Women

Only women of non-childbearing potential may participate in this study.

Definitions:

Woman of Childbearing Potential
A woman is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

If fertility is unclear (e.g., amenorrhea in adolescents or athletes) and a menstrual cycle cannot be confirmed before first dose of study intervention, additional evaluation should be considered.

Woman Not of Childbearing Potential

Women in the following categories are not considered woman of childbearing potential

1. Premenarchal
2. Premenopausal female with 1 of the following:
    - Documented hysterectomy
    - Documented bilateral salpingectomy
    - Documented bilateral oophorectomy

For individuals with permanent infertility due to an alternate medical cause other than the above, (e.g., mullerian agenesis, androgen insensitivity), investigator discretion should be applied to determining study entry.

Note: Documentation can come from the site personnel's: review of the participant's medical records, medical examination, or medical history interview.

3. Postmenopausal female is defined as, women with
    - 12 months of amenorrhea for women >55 years, with no need for follicle-stimulating hormone (FSH)
    - 12 months of amenorrhea for women >40 years with FSH ≥40 mIU/mL and no other medical condition such as anorexia nervosa and not taking medications during the amenorrhea (e.g. oral contraceptives, hormones, gonadotropin-releasing hormone, anti-estrogens, selective estrogen receptor modulators, or chemotherapy that induced amenorrhea)

10.4.2. Men

Men, regardless of their fertility status, must agree to either remain abstinent (if this is their preferred and usual lifestyle) or use condoms as well as 1 additional highly effective method of contraception (less than 1% failure rate) or effective method of contraception with nonpregnant women of childbearing potential partners for the duration of the study and until their plasma concentrations are below the level that could result in a relevant potential exposure to a possible fetus, predicted to be 140 days after the last dose.

Men with pregnant partners should use condoms during intercourse for the duration of the study and until the end of estimated relevant potential exposure to the fetus, predicted to be 140 days after the last dose.

Acceptable Methods of Contraception for Female Partners of Male Participants

Highly effective methods of contraception (less than 1% failure rate) comprise, but are not limited to

- combination oral contraceptives
- implanted contraceptives, or
- intrauterine devices.

Effective methods of contraception comprise but are not limited to diaphragms with spermicide or cervical sponges.

Men and their partners may choose to use a double–barrier method of contraception that must include use of a spermicide.

10.4.3. Collection of Pregnancy Information

Male participants with partners who become pregnant

The investigator will attempt to collect pregnancy information on any male participant's female partner who becomes pregnant while the male participant is in this study. This applies only to male participants who receive study intervention.

After obtaining the necessary signed informed consent from the pregnant female partner directly, the investigator will record pregnancy information on the appropriate form and submit it to the sponsor within 24 hours of learning of the partner's pregnancy.

The female partner will also be followed up to determine the outcome of the pregnancy. Information on the status of the mother and child will be forwarded to the sponsor. Generally, the follow-up will be no longer than 6 to 8 weeks following the estimated delivery date. Any termination of the pregnancy will be reported including fetal status (presence or absence of anomalies) and indication for the procedure.

Female participants who become pregnant

The investigator will collect pregnancy information on any female participant who becomes pregnant while participating in this study. The initial information will be recorded on the appropriate form and submitted to the sponsor within 24 hours of learning of a participant's pregnancy.

The participant will be followed up to determine the outcome of the pregnancy. The investigator will collect follow-up information on the participant and the neonate and the information will be forwarded to the sponsor. Generally, follow-up will not be required for longer than 6 to 8 weeks beyond the estimated delivery date. Any termination of pregnancy will be reported, including fetal status (presence or absence of anomalies) or indication for the procedure.

While pregnancy itself is not considered to be an AE or SAE, any pregnancy complication or elective termination of a pregnancy for medical reasons will be reported as an AE or SAE.

A spontaneous abortion (occurring at <20 weeks gestational age) or still birth (occurring at >20 weeks gestational age) is always considered to be an SAE and will be reported as such.

Any poststudy pregnancy-related SAE considered reasonably related to the study intervention by the investigator will be reported to the sponsor as described in Section 8.3.4. While the investigator is not obligated to actively seek this information in former study participants, he or she may learn of an SAE through spontaneous reporting.

10.5. Appendix 5: Genetics

Sample collection information is found in Appendix 2, Section 10.2 (Clinical Laboratory Tests).

Genetic variation may impact a participant's response to study intervention, susceptibility to, and severity and progression of disease. Variable response to study intervention may be due to genetic determinants that impact drug absorption, distribution, metabolism, and excretion; mechanism of action of the drug; disease etiology; and/or molecular subtype of the disease being treated. Therefore, where local regulations and IRB/IEC allow, a blood sample will be collected for DNA analysis from consenting participants.

DNA samples may be used for research related to SARS-CoV-2 and related diseases. They may also be used to develop tests/assays including diagnostic tests related to LY3832479 or SARS-CoV-2. Genetic research may consist of the analysis of 1 or more candidate genes or the analysis of genetic markers throughout the genome as appropriate.

The samples may be analyzed as part of a multistudy assessment of genetic factors involved in the response to LY3832479 or study interventions of this class to understand study disease or related conditions.

The results of genetic analyses may be reported in the clinical study report or in a separate study summary.

The sponsor will store the DNA samples in a secure storage space with adequate measures to protect confidentiality.

The samples will be retained at a facility selected by the sponsor or its designee while research on SARS-CoV-2 continues but no longer than 15 years or other period as per local requirements.

10.6. Appendix 6: Liver Safety: Suggested Actions and Follow-Up Assessments

Hepatic Evaluation Testing

See Section 8.2.4 for guidance on appropriate test selection.

Testing will be performed locally.

Hematology	**Clinical Chemistry**
Hemoglobin	Total bilirubin
Hematocrit	Direct bilirubin
Erythrocytes (RBCs - red blood cells)	Alkaline phosphatase (ALP)
Leukocytes (WBCs - white blood cells)	Alanine aminotransferase (ALT)
Differential:	Aspartate aminotransferase (AST)
Neutrophils, segmented	Gamma-glutamyl transferase (GGT)
Lymphocytes	Creatine kinase (CK)
Monocytes	**Other Chemistry**
Basophils	Acetaminophen
Eosinophils	Acetaminophen protein adducts
Platelets	Alkaline phosphatase isoenzymes
Cell morphology (RBC and WBC)	Ceruloplasmin
	Copper
Coagulation	Ethyl alcohol (EtOH)
Prothrombin time, INR (PT-INR)	Haptoglobin
Serology	Immunoglobulin IgA (quantitative)
Hepatitis A virus (HAV) testing:	Immunoglobulin IgG (quantitative)
HAV total antibody	Immunoglobulin IgM (quantitative)
HAV IgM antibody	Phosphatidylethanol (PEth)
Hepatis B virus (HBV) testing:	**Urine Chemistry**
Hepatitis B surface antigen (HBsAg)	Drug screen
Hepatitis B surface antibody (anti-HBs)	Ethyl glucuronide (EtG)
Hepatitis B core total antibody (anti-HBc)	**Other Serology**
Hepatitis B core IgM antibody	Anti-nuclear antibody (ANA)
Hepatitis B core IgG antibody	Anti-smooth muscle antibody (ASMA) [a]
HBV DNA [c]	Anti-actin antibody [b]
Hepatis C virus (HCV) testing:	Epstein-Barr virus (EBV) testing:
HCV antibody	EBV antibody

HCV RNA [c]	EBV DNA [c]
Hepatitis D virus (HDV) testing:	Cytomegalovirus (CMV) testing:
HDV antibody	CMV antibody
Hepatitis E virus (HEV) testing:	CMV DNA [c]
HEV IgG antibody	Herpes simplex virus (HSV) testing:
HEV IgM antibody	HSV (Type 1 and 2) antibody
HEV RNA [c]	HSV (Type 1 and 2) DNA [c]
Microbiology	Liver kidney microsomal type 1 (LKM-1) antibody
Culture:	
Blood	
Urine	

[a] Not required if anti-actin antibody is tested.

[b] Not required if anti-smooth muscle antibody (ASMA) is tested.

[c] Reflex/confirmation dependent on regulatory requirements, testing availability, or both.

10.7. Appendix 7: Recommended Laboratory Testing for Hypersensitivity Events

Laboratory assessments should be performed if the participant experiences generalized urticaria or if anaphylaxis is suspected.

- Collect sample after the participant has been stabilized, and within 1 to 2 hours of the event; however, samples may be obtained as late as 12 hours after the event as analytes can remain altered for an extended period of time. Record the time at which the sample was collected.
- Obtain a follow-up sample after approximately 4 weeks.

Clinical Laboratory Tests for Hypersensitivity Events

Hypersensitivity Tests	**Notes** Selected test may be obtained in the event of anaphylaxis or systemic allergic/hypersensitivity reactions.
LY3832479 antidrug antibodies (immunogenicity/ADAs)	Assayed by Lilly-designated laboratory. Results will not be provided to the study sites.
LY3832479 concentrations (PK)	Assayed by Lilly-designated laboratory. Results will not be provided to the study sites.
Tryptase	Assayed by Lilly-designated laboratory. Results will not be provided to the study sites. The study site should attempt to obtain a tryptase sample within 2 hours of the event. If more than 12 hours have passed since the event, no tryptase sample should be obtained. If the tryptase sample is obtained between 2 and 12 hours, or is not obtained, the site should collect a urine sample for N-methylhistamine testing. Collect the first void urine following the event. Collect a follow-up urine sample after approximately 4 weeks.
N-methylhistamine	Assayed by Lilly-designated laboratory. Results will not be provided to the study sites.
Drug-specific IgE	Will be performed if a validated assay is available. Assayed by Lilly-designated laboratory. Results will not be provided to the study sites.
Basophil activation test	Will be performed if a validated assay is available. Assayed by Lilly-designated laboratory. Results will not be provided to the study sites. **NOTE:** The basophil activation test is an in vitro cell-based assay that only requires a serum sample. It is a surrogate assay for drug specific IgE but is not specific for IgE.
Complement (C3, C3a and C5a)	Assayed by Lilly-designated laboratory. Results will not be provided to the study sites.
Cytokine panel	Assayed by Lilly-designated laboratory. Results will not be provided to the study sites.

Abbreviations: IgE = immunoglobulin E; PK = pharmacokinetics.

10.8. Appendix 8: Abbreviations

Term	Definition
ACE2	angiotensin-converting enzyme 2
ADA	antidrug antibody
ADE	antibody-dependent enhancement
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
blinding	A double-blind study is 1 in which neither the participant nor any of the investigator or sponsor personnel who are involved in the treatment or clinical evaluation of the participants are aware of the treatment received.
BMI	body mass index
BP	blood pressure
CFR	Code of Federal Regulations
CK	creatine kinase
CMV	cytomegalovirus
CT	computed tomography
Complaint	A complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, purity, durability, reliability, safety or effectiveness, or performance of a drug or drug delivery system.
compliance	Adherence to all study-related, good clinical practice (GCP), and applicable regulatory requirements.
COVID-19	coronavirus disease 2019
CRP	clinical research physician: Individual responsible for the medical conduct of the study. Responsibilities of the CRP may be performed by a physician, clinical research scientist, global safety physician, or other medical officer.
CRU	clinical research unit
D. Bil	direct bilirubin
EBV	Epstein-Barr virus
ECG	electrocardiogram

eCRF	electronic case report form
EDC	electronic data capture
enroll	The act of assigning a participant to a treatment. Participants who are enrolled in the study are those who have been assigned to a treatment.
enter	Participants entered into a study are those who sign the informed consent form directly or through their legally acceptable representatives.
ERCP	endoscopic retrograde cholangiopancreatography
FSH	follicle-stimulating hormone
GCP	good clinical practice
GGT	gamma-glutamyltransferase
GLP	good laboratory practice
HCV	hepatitis C virus
HDV	hepatitis D virus
HIV	human immunodeficiency virus
IB	Investigator's Brochure
ICF	informed consent form
ICH	International Council for Harmonisation
IEC	independent ethics committee
Ig	immunoglobulin
informed consent	A process by which a participant voluntarily confirms his or her willingness to participate in a particular study, after having been informed of all aspects of the study that are relevant to the participant's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.
intervention	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including products already on the market when used or assembled (formulated or packaged) in a way different from the authorized form, or marketed products used for an unauthorized indication, or marketed products used to gain further information about the authorized form.
INR	international normalized ratio
IRB	institutional review board
IV	intravenous
mAb	monoclonal antibody

MRCP	magnetic resonance cholangiopancreatography
participant	Equivalent to CDISC term “subject”: an individual who participates in a clinical trial, either as recipient of an investigational medicinal product or as a control
PK/PD	pharmacokinetics/pharmacodynamics
PT	prothrombin time
RBD	receptor-binding domain
SAE	serious adverse event
SAP	statistical analysis plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
screen	The act of determining if an individual meets minimum requirements to become part of a pool of potential candidates for participation in a clinical study.
SoA	Schedule of Activities
TBL	total bilirubin
TCR	tissue cross-reactivity
TE	treatment emergent
TEAE	Treatment-emergent adverse event: An untoward medical occurrence that emerges during a defined treatment period, having been absent pretreatment, or worsens relative to the pretreatment state, and does not necessarily have to have a causal relationship with this treatment.
TK	toxicokinetic(s)
ULN	upper limit of normal

11. References

Cangelosi RA, Schwartz EJ, Wollkind DJ. A quasi-steady-state approximation to the basic target-cell-limited viral dynamics model with a non-cytopathic effect. Front Microbiol. 2018;9:54.

Division of AIDS (DAIDS) table for grading the severity of adult and pediatric adverse events. National Institute of Allergy and Infectious Diseases. National Institutes of Health. US Department of Health and Human Services. Corrected version 2.1. July 2017. Available at: https://rsc.niaid.nih.gov/sites/default/files/daidsgradingcorrectedv21.pdf. Accessed May 19, 2020.

[EMA] European Medicines Agency. Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products. 2017. Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-strategies-identify-mitigate-risks-first-human-early-clinical-trials-investigational_en.pdf. Accessed May 19, 2020.

Graham BS. Rapid COVID-19 vaccine development [published online May 08, 2020]. *Science*. doi: 10.1126/science.abb8923.

Hamming I, Timens W, Bulthuis MLC, et al. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J. Pathol*. 2004;203:631-637.

Human Protein Atlas Project website. Available at: https://www.proteinatlas.org/ENSG00000130234-ACE2/tissue. Accessed May 14, 2020.

Kim KS, Ejima K, Ito Y, et al. Modelling SARS-CoV-2 dynamics: implications for therapy. 2020. medRxiv doi: https://doi.org/10.1101/2020.03.23.20040493.

Lieberman P, Nicklas RA, Randolph C, et al. Anaphylaxis – a practice parameter update 2015. *Ann Allergy Asthma Immunol*. 2015; 115:341-384.

Magyarics Z, Leslie F, Bartko J, et al. Randomized, double-blind, placebo-controlled, singleascending-dose study of the penetration of a monoclonal antibody combination (ASN100) targeting Staphylococcus aureus cytotoxins in the lung epithelial lining fluid of healthy volunteers. Antimicrob Agents Chemoter. 2019;63(8). pii:e00350-19.

Simons FER, Ebisawa M, Sanchez-Borges M, et al. 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. *World Allergy Organ J*. 2015;8:32.

Shah Dk, Betts AM. Antibody biodistribution coefficients: inferring tissue concentrations of monoclonal antibodies based on the plasma concentrations in several preclinical species and human. MAbs. 2013;5(2):297-305.

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