2. SYNOPSIS

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Study Title:
A Double blind Phase 1/2 study of S-268019

Investigators and Study Centers:
This study was a single-center study conducted in Japan.

Publication (reference): Not applicable

Studied Period:
From 04 Aug 2021 to 15 Sep 2022 (the date of the last-participant-last-visit)

Phase of Development: Phase 1/2

Objectives and Endpoints:

Objectives	Endpoints
Primary	
• To assess the safety and tolerability of S-268019-b in healthy Japanese adults.	• Incidence of adverse events (AEs)/treatment-related AEs/serious AEs (SAEs)/solicited AEs, vital signs, laboratory tests, and 12-lead electrocardiograms (ECGs)
Secondary	
• To assess the immunogenicity of S-268019-b in healthy Japanese adults.	• The following items for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) neutralizing antibody titer and anti-spike protein immunoglobulin G (IgG) antibody titer − Geometric mean titer (GMT) − Geometric mean fold rise (GMFR) − Seroconversion rate
Exploratory	
• To assess other immunological indices.	• Cellular immunity − Cytokine-producing cell count • Type 1 helper T cells (Th1)/Type 2 helper T cells (Th2) balance − T cell cytokine assay • Gene analysis of B cell and T cell receptors • Biomarkers

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Methodology: This study was a single-center, randomized, double-blind, placebo-controlled study in healthy Japanese adults (aged 20 to 64 years). The study consisted of 3 groups: S-268019-b 5 µg group, S-268019-b 10 µg group, and placebo group. The target sample size was up to 60 participants (24 participants × 2 in the S-268019-b groups [S-268019-b 5 µg group or S-268019-b 10 µg group] and 12 participants in the placebo group).

Because this was the first administration of S-268019-b in humans, administration was started with 2 participants at first (S-268019-b 5 µg group, 1 participant; S-268019-b 10 µg group, 1 participant). The study intervention had to be given to the second participant at least 1 hour after study intervention for the first participant. As the 2 participants had not experienced any serious treatment-related AEs (AEs considered to be "related" to the study intervention) by the visit on the next day of the first administration of study intervention, additional 8 participants (S-268019-b 5 µg group, 3 participants; S-268019-b 10 µg group, 3 participants; placebo group, 2 participants) were allowed to receive the study intervention. As both of the following criteria were met, further additional 50 participants were allowed to receive the study intervention. If an event that did not meet either of the following criteria occurred, the Data and Safety Monitoring Board was to be convened to confirm the safety results in an unblinded manner, and then was to be judged the acceptability of enrolling the additional participants.

- No serious treatment-related AEs (AEs considered to be "related" to the study intervention) occurred by 3 days after the first administration of study intervention (Day 4) in the S-268019-b groups of the applicable dose.
- Grade 3 or higher treatment-related AEs (Common Terminology Criteria for Adverse Events [CTCAE] version 5.0) occurred in less than 2 participants by 3 days after the first administration of study intervention (Day 4) in the S-268019-b groups.

Out of the participants assigned to the S-268019-b 5 µg group and the S-268019-b 10 µg group, those who wanted to receive the third study intervention were allowed to receive S-268019-b 10 µg on Day 204. However, if a participant met any of the following criteria, the third study intervention was prohibited.

- The participant was found to be infected with SARS-CoV-2 on the basis of antigen test or reverse transcription polymerase chain reaction (RT-PCR) test

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during the period from the first administration of study intervention to Day 204 pre-dose.

- When any of the following conditions was met in ECG during the period from the first administration of study intervention to Day 204 pre-dose:
  - QTc interval corrected using Fridericia's correction formula (QTcF) was > 500 msec or uncorrected QT > 600 msec.
  - QTcF change from baseline > 60 msec.

- The participant received any approved SARS-CoV-2 vaccine during the period from the first administration of study intervention to Day 204 pre-dose.
- The participant became pregnant during the period from the first administration of study intervention to Day 204 pre-dose.
- A serious or intolerable AE occurred during the period from the first administration of study intervention to Day 204 pre-dose and the investigator or subinvestigator considered that the third administration of study intervention was not to be administered.
- Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) was ≥ 3 × upper limit of normal (ULN) during the period from the first administration of study intervention to Day 204 pre-dose.

The study was composed of the following 3 periods:

- Screening period (Day −14 to Day −1):

  Individuals who had provided informed consent were screened to confirm their eligibility for participation in the study.
- Evaluation period (Day 1 to Day 50 [28 ± 3 days after Visit 6]):

  Individuals who were confirmed eligible to participate in the study on Day 1 were randomly assigned pre-dose to the S-268019-b 5 μg group, the S-268019-b 10 μg group, or the placebo group. For primary vaccination, participants received one dose each of the assigned study intervention via intramuscular injection at the study site on Day 1 and Day 22. The pre- and post-dose investigations/examinations were performed as scheduled. Participants also visited the study site on Days 2, 4, 8, 15, 29, 36, and 50 (Day 2 and Day 4 were essential for the first 10 vaccinated participants only and were to be conducted for additional 50 participants only when follow-up was necessary) to undergo investigations/examinations as scheduled.

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- Follow-up period (Day 51 [the day after Visit 9] to Day 386 [364 ± 14 days after Visit 6]):

  Participants visited the study site on Days 113, 204, 218, 232, 295, and 386 (only participants who received the third study intervention on Day 204 visited on Day 218 and Day 232) to undergo the scheduled investigations/examinations. For booster vaccination, out of the participants assigned to the S-268019-b 5 μg group and the S-268019-b 10 μg group, those who wanted to receive the third study intervention received S-268019-b 10 μg intramuscularly once at the study site on Day 204.

This final clinical study report (CSR) was prepared with the results of final analyses using the data from all participants up to the final visit in the study.

Number of Participants (Planned and Analyzed):

Planned: Up to 60 participants (24 participants × 2 in the S-268019-b groups [S-268019-b 5 μg or S-268019-b 10 μg] and 12 participants in the placebo group).

Randomized: 60 (24 in the S-268019-b 5 μg group, 24 in the S-268019-b 10 μg group, 12 in the placebo group)

Analyzed for immunogenicity:

- Full analysis set (FAS): 60 (24 in the S-268019-b 5 μg group, 24 in the S-268019-b 10 μg group, 12 in the placebo group)

Analyzed for efficacy:

Not applicable.

Analyzed for safety:

- Safety analysis population: 60 (24 in the S-268019-b 5 μg group, 24 in the S-268019-b 10 μg group, 12 in the placebo group)

Diagnosis and Main Criteria for Inclusion:

1. Inclusion criteria

- Japanese healthy adult male or female participants, who were 20 to 64 years of age inclusive, at the time of signing the informed consent form (ICF).
- Body mass index (BMI) had to be within the range of 18.5 to 25.0 (inclusive) at screening.

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2. Exclusion criteria

- Participants who were not healthy, were not able to comply with study requirements, received any approved or investigational SARS-CoV-2 vaccine, participated in any other clinical study within 30 days.

Diagnostic Assessments

- Positive for SARS-CoV-2 infection (as determined by SARS-CoV-2 antigen test) at screening or before the first administration of study intervention on Visit 1 (Day 1).

Medical Conditions

- Current history of cardiovascular, respiratory, hepatic, renal, gastrointestinal, endocrine, hematological, or neurological disease that, in the opinion of the investigator or subinvestigator, would constitute a safety concern or confound data interpretation.
- A fever ≥ 37.5°C on the day of the first administration of study intervention.
- Positive SARS-CoV-2 antibody test at screening or a known history of SARS-CoV-2 infection as determined by medical interview before the first administration of study intervention.
- Contraindicated for intramuscular vaccination or blood collection.

Other Exclusions

- Individuals considered to have hypersensitivity to any of the study interventions or components thereof, or drug or other allergy that, in the opinion of the investigator or subinvestigator, contraindicates participation in the study (except for pollinosis and atopic dermatitis).
- Ineligibility for the study as considered by the investigator or subinvestigator.

Test Product, Dose and Mode of Administration, Lot Number:

1. Test Product

S-268019 injectable (containing S-910823) 20 μg/mL (antigen), S-268019 injectable (containing S-910823) 40 μg/mL (antigen), and S-268019 oil in water emulsion for injection 1 mL (adjuvant)

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2. Dose and Mode of Administration

For primary vaccination, S-268019-b (injectable emulsion) was prepared at the time of use by mixing S-910823 (antigen) with A-910823 (adjuvant, oil in water emulsion for injection) at a 1:1 ratio and injected. A-910823 0.75 mL from the vial of 1 mL of A-910823 was taken, and then added to the vial filled with 0.75 mL of S-268019 for injection which contained S-910823 at 20 μg/mL or 40 μg/mL. One dose (0.5 mL) was given in the upper arm intramuscularly at a 3-week interval for a total of two doses.

For booster vaccination, S-268019-b (injectable emulsion) was prepared at the time of use by mixing S-910823 (antigen) with A-910823 (adjuvant, oil in water emulsion for injection) at a 1:1 ratio and injected. A-910823 0.75 mL from the vial of 1 mL of A-910823 was taken, and then added to the vial filled with 0.75 mL of S-268019 for injection which contained S-910823 at 40 μg/mL. One dose (0.5 mL) was given in the upper arm intramuscularly once.

3. Packaging Lot Number

[redacted] (S-268019 injectable [containing S-910823] 20 μg/mL [antigen])
[redacted] (S-268019 injectable [containing S-910823] 40 μg/mL [antigen])
[redacted] (S-268019 injectable [containing S-910823] 40 μg/mL [antigen])
[redacted] (S-268019 oil in water emulsion for injection 1 mL [adjuvant])
[redacted] (S-268019 oil in water emulsion for injection 1 mL [adjuvant])

Duration of Treatment:

Primary vaccination: 2 days (one dose of S-268019-b 5 μg or 10 μg was injected twice at a 3-week interval)

Booster vaccination (if applicable): 1 day (one dose of S-268019-b 10 μg was injected once)

Reference Therapy, Dose and Mode of Administration, Lot Number:

1. Reference Therapy

S-268019 placebo injectable (saline)

2. Dose and Mode of Administration

0.5 mL each of the placebo was injected intramuscularly in the upper arm at a 3-week interval for a total of two doses.

3. Packaging Lot Number

[redacted]

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Criteria for Evaluation:
Immunogenicity and Other Immunological Indices Assessment:

There were no criteria set for evaluation of immunogenicity or other immunological indices.

Efficacy Assessment:

Not applicable.

Safety Assessment:

A treatment-emergent AE (TEAE) was defined as an AE occurring after the first administration of study intervention. Treatment-related AE was defined as AEs considered to be "related" to the study intervention.

The following AEs were defined as the solicited AEs (solicited systemic AEs and solicited local AEs) which occurred within 7 days after each vaccination in this study. Solicited systemic treatment-related AEs, solicited local treatment-related AEs, and unsolicited treatment-related AEs were defined as the solicited systemic AEs, solicited local AEs, and unsolicited AEs considered to be "related" to the study intervention, respectively.

- Solicited systemic AEs:
  - Fever
  - Nausea/vomiting
  - Diarrhea
  - Headache
  - Fatigue
  - Myalgia
- Solicited local AEs:
  - Pain
  - Erythema/redness
  - Induration
  - Swelling

Potential immune-mediated diseases were collected as the AEs of special interest (AESIs) of S-268019. Details of AESIs are provided in Section 9.5.1.4.3.

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Statistical Methods:

Immunogenicity Analyses:

The following immunogenicity analyses were performed for FAS. The analysis methods for immunogenicity endpoints were as follows:

- GMT of SARS-CoV-2 neutralizing antibody and anti-spike protein IgG antibody at each time point

  The GMT and the corresponding 95% confidence interval (CI) were calculated for each intervention group by back transformation of the arithmetic mean and its 95% CIs of the log-transformed titers. The GMT ratio and the corresponding 95% CI were estimated for each pairwise comparison of S-268019-b groups by back transformation of the difference between interventions and its 95% CI which were obtained using an analysis of covariance (ANCOVA) model fitted on the log-transformed antibody titers of S-268019-b groups at each time point. The model included intervention group as a fixed effect as well as age (continuous) as a covariate.
- GMFR of SARS-CoV-2 neutralizing antibody titer and anti-spike protein IgG antibody titer at each time point

  The GMFR and the corresponding 95% CI were calculated for each intervention group by back transformation of the arithmetic mean and its 95% CIs of the change from baseline in log-transformed titers. The GMFR ratio and the corresponding 95% CI were estimated for each pairwise comparison of S-268019-b groups by back transformation of the difference between interventions and its 95% CI which were obtained using an ANCOVA model fitted on the change from baseline in log-transformed antibody titers of S-268019-b groups. The model included intervention group as a fixed effect as well as age (continuous) as a covariate.
- SARS-CoV-2 neutralizing antibody titer seroconversion rate and anti-spike protein IgG antibody titer seroconversion rate at each time point

  The proportion of participants with a ≥ 4-fold rise from baseline in each antibody titer (seroconversion) and its 95% CI were calculated for each intervention group and at each time point. The 95% CI for antibody titer seroconversion rate was calculated using the Clopper-Pearson method. The odds ratio and the corresponding 95% CI were estimated for each pairwise comparison between S-268019-b groups using logistic regression model fitted on each antibody titer seroconversion rate in the S-268019-b groups at each

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time point. The model included intervention group as a fixed effect as well as age (continuous) as a covariate.

Efficacy Analyses:

Not applicable.

Safety Analyses:

The following safety analyses were performed for the safety analysis population.

AEs were coded and classified by system organ class (SOC) and preferred term (PT) using the Medical Dictionary for Regulatory Activities (MedDRA) Version 24.0. The number and percentage of participants with AEs, death, other SAEs, AESIs, AE leading to discontinuation, solicited systemic AEs, solicited local AEs, and unsolicited AEs (events other than solicited systemic AEs or solicited local AEs) were summarized by intervention group. The incidences and their 95% CIs were calculated by using the Clopper-Pearson method. The number of cases of these AEs were also presented. Treatment-related AEs were summarized in the same manner as AEs.

Summary statistics for laboratory test results, vital signs, 12-lead ECG measurements, and the change from baseline at each scheduled time point were presented by intervention group.

Summary of Results:

Demographics:

Nearly half of the participants were male (45.8% in the S-268019-b 5 μg group, 54.2% in the S-268019-b 10 μg group, and 41.7% in the placebo group; in the same order hereinafter). The mean age (min-max, standard deviation [SD]) was 43.0 (25-61, 9.9) years, 47.1 (26-59, 9.7) years, and 48.0 (28-57, 8.6) years, respectively. The mean BMI (SD) was 21.26 (2.03), 22.21 (1.55), and 21.44 (1.78), respectively. No substantial differences were observed among intervention groups except for habits of drinking (54.2%, 58.3%, and 16.7%, respectively).

Immunogenicity:

The immunogenicity assessments showed that the GMTs of SARS-CoV-2 neutralizing antibody and anti-spike protein IgG antibody increased from baseline both in the S-268019-b 5 μg group and the S-268019-b 10 μg group on Day 50 (28 days after the second administration) and on Days 232, 295, and 386 (28, 91, and 182 days, respectively, after the third administration). The GMTs of SARS-CoV-2 neutralizing antibody and anti-spike protein IgG antibody in the S-268019-b 5 μg group and S-268019-b 10 μg group after the third administration (on Days 232, 295,

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and 386 [28, 91, and 182 days, respectively, after the third administration]) were higher than the maximum GMT after the second administration (on Day 36 [14 days after the second administration]).

- GMT of SARS-CoV-2 neutralizing antibody at each time point
  After 2 injections of the study intervention administered for primary vaccination, the GMTs of SARS-CoV-2 neutralizing antibody (measured at [redacted] increased from Day 1 to Days 36 and 50 in the S-268019-b groups. The maximum GMTs of SARS-CoV-2 neutralizing antibody in the S-268019-b 5 μg group and the S-268019-b 10 μg group were observed on Day 36 and the maximum GMT was higher in the S-268019-b 10 μg group than in the S-268019-b 5 μg group.
  After 1 injection of the S-268019-b 10 μg administered on Day 204 for booster vaccination, the GMT of SARS-CoV-2 neutralizing antibody further increased from Day 204 to Days 218, 232, 295, and 386 in the S-268019-b groups. The maximum GMTs of SARS-CoV-2 neutralizing antibody in the S-268019-b 5 μg group and the S-268019-b 10 μg group were observed on Day 218 and were comparable between the S-268019-b groups.
- GMFR of SARS-CoV-2 neutralizing antibody titer at each time point
  After 2 injections of the study intervention administered for primary vaccination, the GMFRs (95% CIs) of SARS-CoV-2 neutralizing antibody titer (measured at [redacted] in the S-268019-b 5 μg group, the S-268019-b 10 μg group, and the placebo group were 14.67 (10.25 to 21.01), 18.49 (13.89 to 24.61), and 1.00 (not calculated), respectively, on Day 36, and 8.48 (6.14 to 11.70), 11.31 (8.61 to 14.86), and 1.00 (not calculated), respectively, on Day 50.
  After 1 injection of the S-268019-b 10 μg administered on Day 204 for booster vaccination, the GMFRs (95% CIs) of SARS-CoV-2 neutralizing antibody titer in the S-268019-b 5 μg group and the S-268019-b 10 μg group were 71.01 (51.54 to 97.85) and 74.92 (58.36 to 96.17), respectively, on Day 218, 61.82 (42.01 to 90.97) and 66.05 (52.90 to 82.46), respectively, on Day 232, 51.42 (34.93 to 75.69) and 51.33 (41.19 to 63.97), respectively, on Day 295, and 23.52 (14.20 to 38.95) and 32.00 (21.29 to 48.10), respectively, on Day 386.
- SARS-CoV-2 neutralizing antibody titer seroconversion rate at each time point
  After 2 injections of the study intervention administered for primary

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vaccination, the seroconversion rates (95% CIs) for SARS-CoV-2 neutralizing antibody titer (measured at [redacted] in the S-268019-b 5 μg group, the S-268019-b 10 μg group, and the placebo group were 91.7% (73.0% to 99.0%), 100.0% (85.8% to 100.0%), and 0.0% (0.0% to 26.5%), respectively, on Days 36 and 50.
After 1 injection of the S-268019-b 10 μg administered on Day 204 for booster vaccination, the seroconversion rates (95% CIs) for SARS-CoV-2 neutralizing antibody titer in the S-268019-b 5 μg group and the S-268019-b 10 μg group were 100.0% (83.2% to 100.0%) and 100.0% (84.6% to 100.0%), respectively, on Days 218 and 232, 100.0% (82.4% to 100.0%) and 100.0% (84.6% to 100.0%), respectively, on Day 295, and 100.0% (81.5% to 100.0%) and 100.0% (83.2% to 100.0%), respectively, on Day 386.

- GMT of anti-spike protein IgG antibody at each time point
  After 2 injections of the study intervention administered for primary vaccination, the GMTs of anti-spike protein IgG antibody increased from Day 1 to Days 36 and 50 in the S-268019-b groups.
  The maximum GMTs of anti-spike protein IgG antibody in the S-268019-b 5 μg group and the S-268019-b 10 μg group were observed on Day 36 and the maximum GMT was higher in the S-268019-b 10 μg group than in the S-268019-b 5 μg group.
  After 1 injection of the S-268019-b 10 μg administered on Day 204 for booster vaccination, the GMTs of anti-spike protein IgG antibody further increased from Day 204 to Days 218, 232, 295, and 386 in the S-268019-b groups. The maximum GMTs of anti-spike protein IgG antibody in the S-268019-b 5 μg group and the S-268019-b 10 μg group were observed on Day 218 and were comparable between the S-268019-b groups.
- GMFR of anti-spike protein IgG antibody titer at each time point
  After 2 injections of the study intervention administered for primary vaccination, the GMFRs (95% CIs) of anti-spike protein IgG antibody titer in the S-268019-b 5 μg group, the S-268019-b 10 μg group, and the placebo group were 527.00 (375.27 to 740.10), 767.13 (555.95 to 1058.53), and 1.00 (not calculated), respectively, on Day 36, and 287.35 (206.47 to 399.91), 469.51 (351.21 to 627.65), and 1.33 (0.90 to 1.98), respectively, on Day 50.
  After 1 injection of the S-268019-b 10 μg administered on Day 204 for booster vaccination, the GMFRs (95% CIs) of anti-spike protein IgG antibody titer in the S-268019-b 5 μg group and the S-268019-b 10 μg group were 3565.78

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(1937.30 to 6563.14) and 2896.31 (2092.45 to 4008.99), respectively, on Day 218, 1217.75 (736.10 to 2014.54) and 1237.08 (977.21 to 1566.06), respectively, on Day 232, 1142.43 (660.09 to 1977.24) and 1317.54 (1015.36 to 1709.66), respectively, on Day 295, and 391.02 (224.19 to 682.02) and 588.13 (388.09 to 891.28), respectively, on Day 386.

- Anti-spike protein IgG antibody titer seroconversion rate at each time point
  After 2 injections of the study intervention administered for primary vaccination, the seroconversion rates (95% CIs) for anti-spike protein IgG antibody titer in the S-268019-b 5 μg group, the S-268019-b 10 μg group, and the placebo group were 100.0% (85.8% to 100.0%), 100.0% (85.8% to 100.0%), and 0.0% (0.0% to 26.5%), respectively, on Day 36, and 100.0% (85.8% to 100.0%), 100.0% (85.8% to 100.0%), and 8.3% (0.2% to 38.5%), respectively, on Day 50.
  After 1 injection of the S-268019-b 10 μg administered on Day 204 for booster vaccination, the seroconversion rates (95% CIs) for anti-spike protein IgG antibody titer in the S-268019-b 5 μg group and the S-268019-b 10 μg group were 100.0% (83.2% to 100.0%) and 100.0% (84.6% to 100.0%), respectively, on Days 218 and 232, 100.0% (82.4% to 100.0%) and 100.0% (84.6% to 100.0%), respectively, on Day 295, and 100.0% (81.5% to 100.0%) and 100.0% (83.2% to 100.0%), respectively, on Day 386.
- The number of interferon-gamma (IFN-γ)-producing cells after the second administration was 10.0-43.2 times as high as that before the first administration (Day 1). And the number of IFN-γ-producing cells after the booster vaccination was 1.99-3.79 times as high as that before the booster vaccination (Day 204), but showing a greater number of IFN-γ-producing cells compared to before the first administration of primary vaccination.
- The IFN-γ-producing cells that respond to the S-268019-b exist even about 6 months after the first administration.
- S-268019-b induced a higher percentage of Th1 cells (which produce IFN-γ or IL-2) than that of Th2 cells (which produce IL-4 or IL-5).

Efficacy:

Efficacy was not assessed in this study.

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Safety:

There were no significant findings of safety or tolerability concern up to Day 386 (364 days after the second administration or 182 days after the third administration) in healthy Japanese adults (aged 25 to 61 years) who received 3 injections of S-268019-b: the first and second administrations of 5 μg or 10 μg at a 3-week interval and the third administration of S-268019-b 10 μg.

No deaths, nonfatal SAEs, AEs leading to discontinuation of study intervention, or AESIs were reported.

A total of 264 AEs were reported in 100.0% (24 of 24) of participants in the S-268019-b 5 μg group, 281 AEs were reported in 100.0% (24 of 24) of participants in the S-268019-b 10 μg group, and 12 AEs were reported in 50.0% (6 of 12) of participants in the placebo group (in the same order hereinafter). A total of 254 treatment-related AEs were reported in 100.0% (24 of 24), 272 treatment-related AEs were reported in 100.0% (24 of 24), and 11 treatment-related AEs were reported in 41.7% (5 of 12). Most of the AEs reported in the S-268019-b groups were considered related to the study intervention. The overall incidences of AEs and treatment-related AEs in the S-268019-b 5 μg were identical to those in the S-268019-b 10 μg group.

The AEs reported in at least 10% of participants in any of the intervention groups were vaccination site pain, fatigue, headache, pyrexia, nausea, myalgia, vaccination site induration, vaccination site swelling, vaccination site erythema, and diarrhoea. All of the AEs reported in at least 10% of participants in any of the intervention groups were considered related to the study intervention except for headache, which was reported in 1 participant each of the S-268019-b 5 μg group and the S-268019-b 10 μg group.

No apparent trends related to the study intervention were found in clinical laboratory tests, vital signs, or ECG parameters in any of the study intervention groups.

Solicited systemic and local AEs:

A total of 132 solicited systemic AEs were reported in 95.8% (23 of 24) of participants in the S-268019-b 5 μg group, 165 solicited systemic AEs were reported in 91.7% (22 of 24) of participants in the S-268019-b 10 μg group, and 5 solicited systemic AEs were reported in 25.0% (3 of 12) of participants in the placebo group (in the same order hereinafter). A total of 130 treatment-related solicited systemic AEs were reported in 95.8% (23 of 24), 164 treatment-related solicited systemic AEs were reported in 91.7% (22 of 24), and 5 treatment-related solicited systemic AEs

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were reported in 25.0% (3 of 12). The overall incidences of solicited systemic AEs and treatment-related solicited systemic AEs in the S-268019-b 5 µg group were similar to those in the S-268019-b 10 µg group. Except for 3 solicited systemic AEs, all other solicited systemic AEs reported in the S-268019-b groups were considered related to the study intervention.

The overall incidences of solicited systemic AEs were higher after the second or third administration than after the first administration in both S-268019-b 5 µg and 10 µg groups. Most of the participants in the S-268019-b groups experienced fatigue after second or third administration of the study intervention. More than half of the participants in the S-268019-b 5 µg group experienced headache after the second or third administration of the study intervention. More than half of the participants in the S-268019-b 10 µg group experienced fever, nausea/vomiting, and headache after the second or third administration of the study intervention.

A total of 123 solicited local AEs were reported in 100.0% (24 of 24), 102 solicited local AEs were reported in 95.8% (23 of 24), and 6 solicited local AEs were reported in 33.3% (4 of 12). A total of 123 treatment-related solicited local AEs were reported in 100.0% (24 of 24), 102 treatment-related solicited local AEs were reported in 95.8% (23 of 24), and 6 treatment-related solicited local AEs were reported in 33.3% (4 of 12). The overall incidences of solicited local AEs and treatment-related solicited local AEs in the S-268019-b 5 µg group were similar to those in the S-268019-b 10 µg group. All of the solicited local AEs reported in the S-268019-b groups were considered related to the study intervention.

No substantial differences in the overall incidences of solicited local AEs were observed between the first, second, and third administrations of the study intervention in either S-268019-b 5 µg or 10 µg group. Most of the participants in the S-268019-b groups experienced pain after each study intervention.

None of the participants experienced Grade 4 or Grade 5 solicited systemic or local AEs. Most of the solicited systemic or local AEs were Grade 1 or Grade 2 in severity for the S-268019-b groups. Overall, most of the solicited systemic and local AEs resolved (considered “recovering/resolving” or “recovered/resolved”) within 4 and 6 days, respectively, after each study intervention. Most of the solicited systemic AEs (fever, nausea/vomiting, diarrhea, headache, fatigue, myalgia) occurred within 3 days after the first, second, or third administration. Most of the solicited local AEs (pain, erythema/redness, induration, swelling) occurred within 2 days after the first, second, or third administration.

Sponsor: Shionogi & Co., Ltd.	**Individual Study Table** **Referring to Part of the Dossier**	***(For National Authority Use only)***
Name of Finished Product Not applicable	**Volume:**	:
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CONCLUSIONS

Immunogenicity Conclusions:

The immunogenicity assessments showed that the GMTs of SARS-CoV-2 neutralizing antibody and anti-spike protein IgG antibody increased from baseline both in the S-268019-b 5 µg group and the S-268019-b 10 µg group on Day 50 (28 days after the second administration) and on Days 232, 295, and 386 (28, 91, and 182 days, respectively, after the third administration). The GMTs of SARS-CoV-2 neutralizing antibody and anti-spike protein IgG antibody in the S-268019-b 5 µg group and S-268019-b 10 µg group after the third administration (on Days 232, 295, and 386 [28, 91, and 182 days, respectively, after the third administration]) were higher than the maximum GMT after the second administration (on Day 36 [14 days after the second administration]).

The number of IFN-γ-producing cells after the second administration was 10.0-43.2 times as high as that before the first administration (Day 1). And the number of IFN-γ-producing cells after the booster vaccination was 1.99-3.79 times as high as that before the booster vaccination (Day 204), but showing a greater number of IFN-γ-producing cells compared to before the first administration of primary vaccination. The IFN-γ-producing cells that respond to the S-268019-b exist even about 6 months after the first administration. S-268019-b induced a higher percentage of Th1 cells (which produce IFN-γ or IL-2) than that of Th2 cells (which produce IL-4 or IL-5).

Efficacy Conclusions:

Efficacy was not assessed in this study.

Safety Conclusions:

There were no significant findings of safety or tolerability concern up to Day 386 (364 days after the second administration or 182 days after the third administration) in healthy Japanese adults (aged 25 to 61 years) who received 3 injections of S-268019-b: the first and second administrations of 5 µg or 10 µg at a 3-week interval and the third administration of S-268019-b 10 µg.

Date of Report: 25 Aug 2023